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# **DELIBERATE SELF-HARM AMONG ADOLESCENTS: COURSE, OUTCOME AND TREATMENT**

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# Deliberate Self-Harm among Adolescents: Course, Outcome & Treatment

## THESIS FOR DOCTORAL DEGREE (Ph.D.)

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Till mamma



# ABSTRACT

**Background:** Self-harm among adolescents is prevalent, and is a risk factor for suicide, which is one of the leading causes of death among youth worldwide. There is a need to better understand the role and impact of self-harm within clinical samples, and the subsequent risks associated with self-harm with and without suicidal intent. Dialectical behavior therapy (DBT) has the strongest empirical support for treatment of self-harm among adolescents, and extended knowledge on important treatment components is critical for the development of brief, efficacious interventions that are easily accessible for adolescents.

**Aim:** The aims were to

- Study clinical and psychosocial correlates as well as long-term outcome among clinical samples with self-harm
- Explore experiences of care among young adults who have participated in specialist-level interventions targeting self-harm (i.e. DBT)

**Methods:** The clinical and psychosocial correlations was studied in a case-control study ( $N = 25,161$ ) comparing three subgroups of patients; 1) self-harm only, 2) self-harm and suicidality, and 3) neither self-harm nor suicidality (controls). Linear regression and logistic regression were used to calculate associations. Outcomes were studied in three different longitudinal cohort studies: 1) outcomes after self-harm with and without suicidal ideation/behavior ( $N = 6,120$ ), 2) outcomes for boys or girls with self-harm ( $N = 110,072$ ), and 3) outcomes after nonsuicidal self-injury (NSSI) or suicide attempt (SA) using NSSI and SA as time-varying covariates ( $N = 2,219$ ). By using Cox regression, Hazard Ratios with 95% Confidence Intervals were estimated for each outcome. Salient treatment components were studied with a qualitative analysis of 19 semi-structured interviews with former DBT patients.

**Results:** Self-harm within clinical populations was associated with higher clinical and psychosocial burden and higher risk of adverse outcomes, e.g. alcohol/substance misuse, violent and nonviolent criminality, as compared with patients with no self-harm. Patients with both self-harm and suicidality are the most vulnerable group. The young self-harming patient valued a therapist who showed explicit concern and trust in the patient's competence to change destructive behaviors, but also meeting and learning from peers.

**Conclusion:** Help-seeking boys and girls with self-harm need appropriate care and assessment, including prevention and treatment of alcohol and substance use. Self-harm might serve as a risk marker for emotion dysregulation and impulsivity within both sexes.

Suicidality in addition to self-harm need to be regularly assessed and signals highly increased risks for future adverse outcomes. Interventions that lower the risks are necessary. Young patients with self-harm, can be strongly motivated, and work hard, to improve their well-being and pursue a life worth living. Teaching and learning from peers might be of particular value and importance among adolescents.



## LIST OF SCIENTIFIC PAPERS

- I. Bjureberg, J., Ohlis, A., Ljótsson, B., D’Onofrio, B. M., Hedman-Lagerlöf, E., Jokinen, J., Sahlin, H., Lichtenstein, P., Cederlöf, M., Hellner, C. (2019). Adolescent self-harm with and without suicidal ideation and behaviors: Cross-sectional and longitudinal analyses of a Swedish regional register. *Journal of Child Psychology and Psychiatry*, 60(3), 295-30.
- II. Ohlis, A., Bjureberg, J., Lichtenstein, P., D’Onofrio, B. M., Fruzzetti, A. E., Cederlöf, M., Hellner, C. (2020). Comparison of suicide risk and other outcomes among boys and girls who self-harm. *European Child & Adolescent Psychiatry*. Advance online publication.
- III. Bjureberg, J., Kuja-Halkola, R., Ohlis, A., Lichtenstein, P., D’Onofrio, B. M., Hellner, C., Cederlöf, M. (manuscript). Adverse clinical outcomes in adolescents with clinician-rated nonsuicidal self-injury and suicide attempt: Longitudinal cohort study
- IV. Ohlis, A., Bjureberg, J., Simonsson, O., Kerj, E., Hallek, C., Fruzzetti, A. E., Cederlöf, M., Hellner, C. (manuscript). Helpful approached from the DBT-A patient’s perspective: A qualitative analysis of former patients’ experiences



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## LIST OF ABBREVIATIONS

ADHD	Attention Deficit Hyperactivity Disorder
ASD	Autism Spectrum Disorder
BPD	Borderline Personality Disorder
CAMHS	Child and Adolescent Mental Health Services
DBT	Dialectical Behavior Therapy
DSH	Deliberate Self-Harm
EUC	Enhanced Usual Care
fMRI	Functional Magnetic Resonance Imaging
HR	Hazard Ratio
ICD-10	International Classification of Diseases
NSSI	Nonsuicidal Self-Injury
OR	Odds Ratio
RCT	Randomized Controlled Trial
SA	Suicide Attempt
SBD	Suicidal Behavior Disorder
SH	Self-Harm
SI	Suicidal Ideation
SU	Suicidal ideation or behaviors
TAU	Treatment as Usual



# 1 INTRODUCTION

During my first year as a resident in child- and adolescent psychiatry I could not sleep. I would lay awake worrying for the self-harming teenage patient, who said she did not want to live anymore, pondering if I could have done something differently or if I had missed something important. I felt her despair, I felt the parents' agony, the siblings' and friends' worry, and I felt ashamed for not being able to help more and better. I did not know what to do, restraints felt wrong, medications did little if anything, and not seldom did the patient's anxiety become too intense even for taking a walk around the block together. Then, one evening, Dr Camilla Hallek from the DBT-unit at CAMHS Stockholm, was being interviewed. She talked about self-harm, and teenagers who had given up on life, and she was not afraid, she knew what to do.

Self-harm is prevalent among adolescents, and while the majority might just try it out a couple of times or so, some develop severe and frequent self-harming behaviors. The most common reasons for self-harm are to escape difficult emotions, or to punish oneself. It is commonly thought of as a dysfunctional strategy for regulating emotions, and is a risk-marker for developing drug use disorders, criminality, and for suicide. Dialectical behavior therapy (DBT) has been found to have effect on self-harm, and among other things, teaches skills to handle difficult emotions. However, DBT is a time-consuming treatment, with limited access for the vast majority of self-harming adolescents.

I wrote an email to Dr Hallek, filled with questions. I doubted she would have time to answer, but fast enough I got a long, informative reply. Dr Hallek became my supervisor, I began working at the DBT-unit and became a DBT-therapist. And I started to sleep again. I was no longer afraid of these encounters; I did not feel helpless. I knew how to validate the patient, help her regulate her anxiety, validate her parents, siblings and friends, and I often knew what needed to be done in order to make the nearest future bearable.

But I still wish I could do more. And I wish it never would have had to go that far, i.e. that the young person never would have had to end up in the CAMHS emergency room or at the DBT-unit. I wish I had the means to intervene earlier. Therefore, I want to learn more about self-harm in adolescents, about correlates, outcomes and treatment interventions. Hence, this thesis. I hope our findings hold elements that future research can build on, with the bridging aim of helping more adolescents prosper. /Anna, Stockholm, October 2020

## 2 BACKGROUND

### 2.1 SELF-HARM, SUICIDAL BEHAVIOR AND SUICIDE AMONG ADOLESCENTS

#### 2.1.1 Definition of self-harm

Non-lethal, self-inflicted, intentional self-harm has throughout history of psychiatry posed a classification challenge, with numerous different terms in use, e.g. self-mutilation, focal suicide, parasuicide, suicide gesture, wrist-cutting syndrome, delicate self-cutting, deliberate self-harm, self-injury, and self-injurious behavior (Chaney, 2012).

The *Dictionary of Psychological Medicine* from 1892 by Daniel Hack Tuke holds a five-page definition of self-mutilation (Chaney, 2012). The psychiatrists at the time distinguished self-mutilation from suicidal behaviors, considering the motives behind the two behaviors to be different (Angelotta, 2015).

More recent studies have shown that a person's intent (suicidal or not) for self-harm can vary both between occasions and during the act (Glenn et al., 2017; Hawton, Saunders, & O'Connor, 2012; Kapur, Cooper, O'Connor, & Hawton, 2013); and it has been questioned if it is possible to distinguish between self-harm without suicidal intent and self-harm with suicidal intent in a reliable manner (Kapur et al., 2013). However, others argue that the distinction is important because prevention strategies and treatment might be different for the diverse subtypes of self-harming behaviors (Bursztein & Apter, 2009; Fox et al., 2015; Muehlenkamp, 2005; Selby, Kranzler, Fehling, & Panza, 2015; Stanford, Jones, & Hudson, 2017).

In the latest version of the Diagnostic and Statistical Manual of Mental Disorders–5 (DSM-5; American Psychiatric Association [APA], 2013), self-harm with and without suicidal intent are included as separate disorders that need further study, unlike the previous version of DSM, where self-harm solely was a symptom of other disorders (Zetterqvist, 2015). Yet, there still is no global consensus regarding the definition and nomenclature for self-harm. This lack of consistency affects the possibility to compare and combine study results, and negatively affects the research progress (Asarnow & Mehlum, 2019; Braun & Clarke, 2016; Clarke, Allerhand, & Berk, 2019; Sedgwick & Ougrin, 2019). There are cross-national differences in defining and naming self-harm, and below I will present the definitions frequently used in Europe and Australia versus in North America.



#### *2.1.1.1 Self-harm*

The term “self-harm” (SH) or “deliberate self-harm” (DSH) are the terms and definitions commonly used in Europe and Australia. SH/DSH do not differentiate between self-harm with or without suicidal intent, i.e. suicide attempts (SA), and includes not only harm to the skin (e.g. cutting, burning, scratching) but also other kinds of self-harming behaviors, as for example self-poisoning (Hawton et al., 2003).

#### *2.1.1.2 Nonsuicidal self-injury*

Nonsuicidal self-injury (NSSI), is the term and definition commonly used in North America and is defined as intentional harm of body tissue without suicidal intent, and for purposes that are not socially sanctioned. It includes behaviors such as cutting, scratching, burning and biting oneself (Nock, 2010). NSSI on five or more days within the last 12 months (and not better accounted for by another disorder/condition), constitutes the NSSI disorder (NSSID), that is included in the DSM-5 under the section Conditions for Further Study (APA, 2013). Also included as a condition for further study, is Suicidal Behavior Disorder (SBD) that comprises suicidal attempts (APA, 2013).

In this literature review, I aim to use the authors’ own chosen terminology in cited studies, yet, when summarizing results from different studies using different terminology, I will choose the terminology that best matches the studies’ definitions. However, my personal approach towards the terminology and definitions have been and still are developing, as can be seen within my own studies in this thesis. My preferred terminology today, partly out of the results from my studies, is the use of NSSI and SA, with self-harm as an overarching term for the combination of NSSI and SA, or for self-harm with unknown intent.

### **2.1.2 Prevalence**

The lack of consensus regarding definition and terminology, and differences in study methodologies (self-report/no self-report, one-item/multi-item report, clinical/non-clinical etc.), cause self-harm prevalence to highly vary between studies and nations (Gillies et al., 2018). Below I summarize the results from some larger meta-analyses and reviews of prevalence studies, as well as results from a European adolescent cohort, a Swedish adolescent cohort, and prevalence found in clinical samples. This is followed by results from studies on gender differences and the global prevalence of suicidal self-harm.

A meta-analysis including 172 community-based samples found the lifetime prevalence of self-harm among adolescents to be 16.9 %, and cutting being the most frequently reported

method (Gillies et al., 2018). The majority (47.1%) reported a lifetime frequency of one or two self-harm incidents, 21.7% reported three to five incidents, 21.6% reported six to 10 incidents, while 5.0% reported > 10 incidents ( $N=68,148$ ; Gillies et al., 2018). A difference in prevalence of DSH (11.4%) and NSSI (22.9%) was found, which is in contrast with findings from a previous review that found no statistically significant difference (Muehlenkamp, Claes, Havertape, & Plener, 2012). A meta-analysis including both community and clinical samples, consisting of 686,672 children and adolescents worldwide, found a similar prevalence (NSSI 22.1%; DSH 13.7%; Lim et al., 2019). The Saving young lives in Europe-project conducted in 11 European countries found that the lifetime prevalence of adolescent self-harm regardless of intent was 27.6% (at least once), 19.7% reported occasional self-harm and 7.8% reported repetitive self-harm (Brunner et al., 2014). In a Swedish community sample of 3,050 adolescents, 35.6% reported that they had self-harmed at least once during the previous 12 months (56.2% among girls; Zetterqvist, Lundh, Dahlstrom, & Svedin, 2013)). Prevalence of the proposed NSSI-disorder (cardinal criteria being NSSI at least 5 days within 12 months) in community samples of adolescents has been reported to be 1.5-6.7% (Zetterqvist, 2015).

In adolescent psychiatric samples the prevalence of self-harm has been reported to be as high as 48–75.9% (Jacobson, Muehlenkamp, Miller, & Turner, 2008; Kaess et al., 2013; Peh et al., 2017).

#### *2.1.2.1 Sex differences*

In meta-analyses, NSSI and self-harm have been found to be more common among females than males (Bresin & Schoenleber, 2015; Gillies et al., 2018), the differences being larger in clinical samples (Bresin & Schoenleber, 2015). In a meta-analysis of studies including Chinese adolescents, sex differences in NSSI prevalence were affected by age, sample type (community or clinical) and area (e.g., urban or rural; Yang & Feldman, 2017). In contrast to the Western findings, NSSI was more prevalent among male college students than among females, although no differences in prevalence were found in clinical samples. Women have been found more likely than men to use some specific methods for self-harm, such as cutting, biting and scratching, while there was no significant difference for other methods like punching (Bresin & Schoenleber, 2015). Yet, in a Swedish clinical cohort, violent methods of self-harm were more common among males than among females (Beckman et al., 2018)

In sexual and gender minorities, the prevalence of NSSI and SA are higher than in the general cisgender population (Butler et al., 2019; Liu et al., 2019; Marshall, Claes, Bouman,

Witcomb, & Arcelus, 2016), 45.5% of the transgender youth reported self-harm within last 12 month in National youth survey in New Zealand (Clark et al., 2014).

#### *2.1.2.2 Suicidal self-harm*

According to the Global Burden of Disease Study 2013, self-harm was the second leading cause of death among males and females aged 10–24 years (Mokdad et al., 2016). Late adolescence and male gender are risk factors for adolescent suicide (Glenn et al., 2020; Keith Hawton & James, 2005; Hawton, Saunders, et al., 2012; Rodway et al., 2016; Roh, Jung, & Hong, 2018). However, in some Asian countries suicide is more common among young females (Bursztein & Apter, 2009; Hawton, Saunders, et al., 2012). In many countries there is a decreasing trend in suicide rates among 10–19 year olds. However, in several European countries this decreasing trend is only found among young males, but not among females where the trends are stable or increasing (Roh et al., 2018). This is also seen in the US, where disparity in suicide rate ratio between males and females is diminishing over time (Curtin, Warner, & Hedegaard, 2016). New Zealand, Estonia and Finland have the highest suicide rates among young people in the age group 10–19, in a comparison with 29 OECD countries, and the US, Korea and Japan have increasing suicide rates in the ages 10-19 (Curtin et al., 2016; Roh et al., 2018). In the US, girls aged 10–14 years had the largest increase in suicide rates between 1999–2014, yet, representing only a small proportion of all suicides in the US (Curtin et al., 2016).

#### **2.1.3 Function**

The function of self-harm has puzzled clinicians and researchers since the nineteenth century, and some proposed motives at the time were not far from today's understanding, for example self-harm as a relief of suffering or an effect of self-hatred (Angelotta, 2015; Chaney, 2012).

The most common function of self-harm, found in different studies, is to escape difficult emotions (Chapman, Gratz, & Brown, 2006; Gillies et al., 2018; Klonsky, 2007; Laye-Gindhu & Schonert-Reichl, 2005; Nock, 2010; Zetterqvist, Lundh, & Svedin, 2013). A review study (including samples of various ages, both clinical and non-clinical; Klonsky, 2007) and a meta-analysis of studies on adolescents in community samples (Gillies et al., 2018), both found emotion regulation to be the most commonly reported reason, followed by self-punishment. Consistently, self-harming behavior is thought to emerge primarily from emotion dysregulation (Gratz & Roemer, 2008; Klonsky, 2007; Nock, 2010).

Nock and Prinstein (2004) proposed a model of four motivational factors for self-harm; 1) automatic negative reinforcement, 2) automatic positive reinforcement, 3) social negative reinforcement and 4) social positive reinforcement. The model has been supported in both clinical and community samples of adolescents (Lloyd-Richardson, Perrine, Dierker, & Kelley, 2007; Nock & Prinstein, 2005; Zetterqvist, Lundh, Dahlstrom, et al., 2013). Although automatic reinforcements, especially automatic negative reinforcement, are the most commonly reported motivational factors (Lloyd-Richardson et al., 2007; Nock & Prinstein, 2005; Nock, Prinstein, & Sterba, 2009; Zetterqvist, Lundh, Dahlstrom, et al., 2013), social reinforcement has also been commonly reported in community samples (Lloyd-Richardson et al., 2007; Zetterqvist, Lundh, Dahlstrom, et al., 2013). It seems as if females are more likely to report automatic functions of self-harm (Victor et al., 2018; Zetterqvist, Lundh, Dahlstrom, et al., 2013), however another study found no gender differences regarding the motivational factors (Lloyd-Richardson et al., 2007).

Two often cited theoretical models of how self-harming behavior develops and is maintained are Nock's (2010) *integrated model* (fig 1) and Chapman et al's (2006) *experiential avoidance model* (EAM; fig 2). Nock's integrated model aims to integrate empirical findings of factors associated with self-harm and describes how these may lead to the development and maintenance of self-harming behavior. As suggested by Nock's model, distal risk factors lead to vulnerability factors that, when matched with a stressful event, evokes unbearable arousal or demands, and together with an NSSI-specific vulnerability factor (untested hypotheses) lead to engaging in NSSI; which in turn is reinforced by regulating either the social situation or the affects (or both; Nock, 2010).

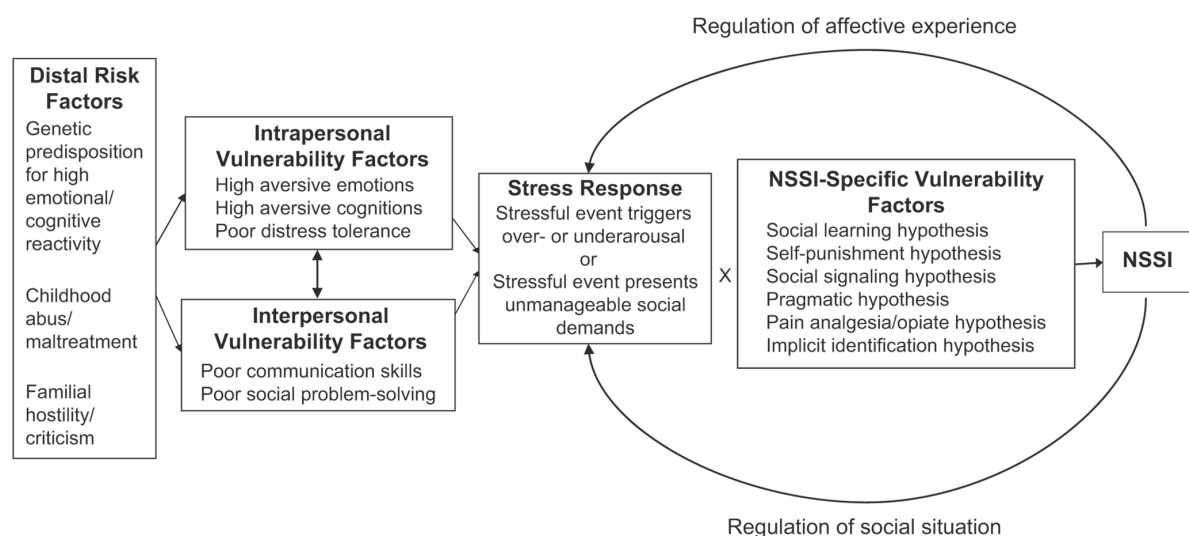


Figure 1: Nock's integrated model. Republished with permission of SAGE Publications, from *Why do people hurt themselves?: New insights into the nature and functions of Self-*

Injury, M. K. Nock, Curr. Dir. Psychol. Sci. 18:78–83, ©2009 by SAGE Publications; permission conveyed through Copyright Clearance Center, Inc.

Chapman et al's model is an evidence based theoretical framework used to explain the maintenance of self-harming behavior, and integrates research on emotions, experiential avoidance and self-harm. In the model, deliberate self-harm is maintained by negative reinforcement due to experiential avoidance of unwanted emotional conditions (Chapman et al., 2006).

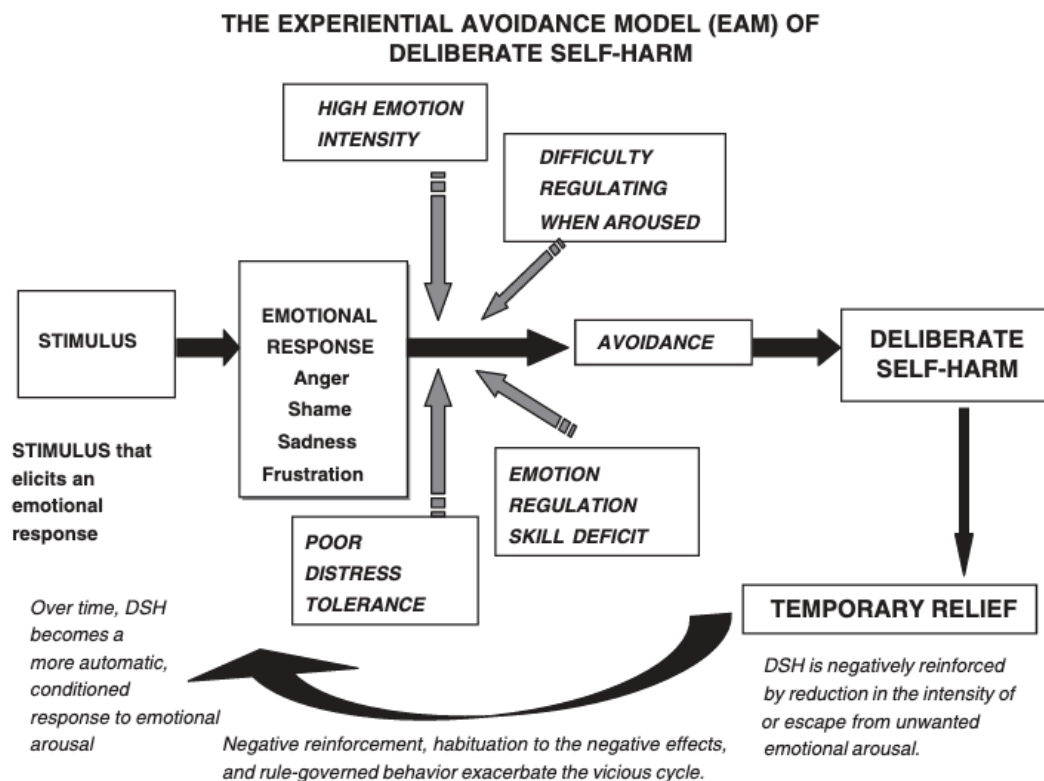


Figure 2: Chapman et al's Experiential Avoidance Model. Reprinted from Behaviour Research and Therapy, Vol 44, Chapman, A.L., Gratz, K. L., & Brown, M. Z., Solving the puzzle of deliberate self-harm: The experiential avoidance model, 371–394, ©2005, with permission from Elsevier.

## 2.1.4 Risk factors

### 2.1.4.1 Longitudinal

In a meta-analysis of risk factors for NSSI, including both adult and adolescent samples (average age 21.32), the overall risk factor strength was weak (Odds Ratio [OR] 1.56, that dropped to 1.16 after adjusting for publication bias; Fox et al., 2015). Regarding specific risk factors, the best predictors of future NSSI were a history of NSSI, cluster B personality

disorder (although large confidence intervals) and hopelessness. However, a significant publication bias was found across the literature concerning risk factors (Fox et al., 2015). The meta-analysis put forward many limitations in the existing literature on risk factors for NSSI, and more longitudinal studies with standardized NSSI measurements, explicit study samples and investigations of novel risk factors are called for, as well as studies examining short-term risk factors, which may be more useful for clinicians in their risk assessments (Fox et al., 2015). In a systematic review, female gender, previous self-harm and symptoms of depression were found to be predictors of self-harm, but again due to heterogeneity in the studies, general conclusions could not be made (Plener, Schumacher, Munz, & Groschwitz, 2015). NSSI has been found to be a robust risk factor for SA (Groschwitz et al., 2015; Mars et al., 2019a; Whitlock et al., 2013), even when controlling for suicidal ideation (SI, (Groschwitz et al., 2015). SI has been found to commonly precede NSSI and SA (Glenn et al., 2017; Groschwitz et al., 2015).

#### *2.1.4.2 Correlates*

Childhood maltreatment is commonly associated with self-harm (Hawton, Saunders, et al., 2012; Kaess et al., 2013; Mars, Heron, Crane, Hawton, Kidger, et al., 2014; Nock, 2010; Plener et al., 2018; Russell et al., 2019). A meta-analysis of childhood maltreatment and NSSI, including both clinical and community samples, analyzed maltreatment overall and subtypes as sexual abuse, and physical or emotional abuse/neglect (Liu, Scopelliti, Pittman, & Zamora, 2018). Childhood maltreatment overall was associated with NSSI (OR 3.42), and among subtypes of childhood maltreatment, emotional abuse had the strongest association (OR 3.03). Across multiple subtypes of maltreatment, stronger associations were found in the non-clinical samples compared to the clinical samples, indicating that maltreatment might be less of a distinguishing factor for NSSI in the clinical population (Liu et al., 2018). Peer victimization and other family related factors (e.g. less parental involvement) are often associated with self-harm (Brunner et al., 2014; Mars, Heron, Crane, Hawton, Kidger, et al., 2014), as is affective disorders, anxiety disorders, substance misuse, PTSD, aggression, impulsivity and cluster B personality disorders (Hawton, Saunders, et al., 2012; Mars, Heron, Crane, Hawton, Lewis, et al., 2014; Plener et al., 2018). Self-harm is common (> 90%; Goodman et al., 2017; Kaess, Brunner, & Chanen, 2014) in adolescents with borderline personality disorder (BPD, a cluster B personality disorder).

#### *2.1.4.3 Differences in correlates for NSSI and SA*

Both community-based and clinical studies have found an overlap of correlating factors associated with SA and NSSI (Andover, Morris, Wren, & Bruzzese, 2012; Hargus, Hawton, & Rodham, 2009; Mars, Heron, Crane, Hawton, Kidger, et al., 2014). Within community samples, some factors have been found more strongly associated with NSSI + SA or SA, e.g.; physical abuse, being bullied, depression, anxiety, suicidal ideation (SI), fewer reasons for living, and self-harm in family (Hargus et al., 2009; Mars, Heron, Crane, Hawton, Kidger, et al., 2014; Muehlenkamp & Gutierrez, 2007), whilst higher novelty seeking has been found to be more strongly associated with NSSI (Mars, Heron, Crane, Hawton, Kidger, et al., 2014). Also some factors have been found to be specific for SA, as e.g. parent suicide attempt and father self-harm, yet this study could not distinguish between SA and the combination of NSSI and SA (Mars, Heron, Crane, Hawton, Lewis, et al., 2014). Within clinical samples, those with both NSSI and SA seem to have more severe symptoms as compared to those with only NSSI or SA (Andover et al., 2012; Stewart et al., 2017). Within a psychiatric inpatient sample about 70% of those adolescents engaging in NSSI reported lifetime SA (Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006). A long history of NSSI, use of different methods and absence of pain was associated with SA among adolescent inpatients with NSSI (Nock et al., 2006). The strongest distinguishing factors between SI and SA have been found to be exposure to self-harm in friends and family (Hargus et al., 2009; Mars et al., 2019b), psychiatric disorders and drug use (Mars et al., 2019b). An anonymous self-report survey of adolescents ( $N = 6,020$ ) found self-harm without suicidal intent to be associated with DSH of a friend, and self-harm with suicidal intent to be associated with DSH of a family member (Hargus et al., 2009). Many of the known risk factors correlated with NSSI and SA are common in the psychiatric clinical populations, however exposure to self-harm among family and friends, and illicit drug use, could have the potential to help inform risk assessment (Hargus et al., 2009; Mars et al., 2019a).

Most studies on clinical correlates to self-harm with and without suicidal intent, are either within community-based samples (Mars, Heron, Crane, Hawton, Kidger, et al., 2014), or based on smaller clinical samples within inpatient settings (Andover et al., 2012; Groholt, Ekeberg, & Haldorsen, 2000; Groschwitz et al., 2015; Nock et al., 2006). Community-based studies are often based on self-reports, vulnerable for biases (e.g. selection bias, recall bias), moreover, the results might not be generalized to a clinical population. Within an inpatient setting, differences in correlates and risk factors between NSSI and SA might be less

pronounced since the population is generally more severely affected. Large studies in clinical cohorts could help advance knowledge regarding clinical correlations with NSSI and SA.

#### *2.1.4.4 Sex differences in correlates to self-harm*

A large cross-sectional study of adolescents in the US (boys n=32,150, girls n=32,521), found associations with other health risks to be similar for boys and girls with NSSI (Monto, McRee, & Deryck, 2018). Yet, in a clinical sample (mean age 17.8) males with NSSI were found to experience fewer negative correlates and less impairment, were more likely to be diagnosed with an unspecified primary diagnosis and less likely to meet the proposed diagnostic criteria for NSSI as compared with females. There was no sex difference in age of onset, wish to stop self-harm, viewing self-harm as a problem, or severity or impulsivity of self-harm (Victor et al., 2018). The associations between psychosocial variables and self-harm have been found to be more strongly correlated among females than males (Brunner et al., 2014; Wan et al., 2019). However, the question arises whether the chosen investigated psychosocial variables could be gender biased from start, and studies on gender specific correlates are sparse.

Identifying as a sexual minority increases the risk for self-harming thoughts and behaviors (Liu et al., 2019), and the risk of displaying a longer and more severe course of the self-harming behavior (Fox et al., 2018). In addition to the commonly reported correlates of self-harm (see above), sexual and gender minorities also have specific risk correlates for NSSI, as internalized homophobia, stigma and discrimination (Liu et al., 2019).

#### *2.1.4.5 Risk profiles*

It has been argued that research on risk factors ought not to be one-dimensional (Stanford et al., 2017). Adolescents who self-harm is a diverse group, and while some only self-harm once and never again, other self-harm frequently and over time. Frequent self-harm and multiple methods are associated with greater psychological distress and more suicidal ideation (Hamza & Willoughby, 2013; Somer et al., 2015; Stanford et al., 2017).

Studying a wide range of correlates, within a large clinical population of adolescents with self-harm, distinguishing between self-harm with and without suicidal intent, could extend upon previous research, and advance knowledge on the groups of adolescents with self-harm that present to the mental health services.



## 2.1.5 Neurobiology

Adolescence is a period of brain development. There are certain behaviors typical for adolescence as risk-taking, impulsivity, self-consciousness and a high susceptibility to peer influence (Blakemore & Mills, 2014). The brain area that undergoes the most striking changes during adolescence is the prefrontal cortex, which is more active during social tasks in adolescents than in adults (Blakemore, 2012). The limbic system of adolescents has been shown to be hypersensitive to the reward feeling of risk-taking, especially among peers (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011). In a review on adolescent brain development and social cognition, Blakemore and Mills (2014) argue that social context and social acceptance influence most of the typical adolescent behaviors.

### 2.1.5.1 *Neuroimaging*

Neuroimaging studies on adolescents and neural correlates to self-harm have increased in the last few years, as pointed out in a recent review (Auerbach, Pagliaccio, Allison, Alqueza, & Alonso, 2020). Apart from structural alterations also differences in neural processing have been found in adolescents with SI, SA and NSSI (Auerbach et al., 2020). For example, altered cortical activation on social exclusion among adolescents with NSSI have been found in fMRI-studies (Brown et al., 2017; Groschwitz, Plener, Groen, Bonenberger, & Abler, 2016; Perini et al., 2019). There are also signs of altered neural processing on emotional stimuli among adolescents with NSSI compared to controls (Plener, Bubalo, Fladung, Ludolph, & Lule, 2012; Westlund Schreiner et al., 2017). By utilizing machine learning approaches, a study among young adults found that neural signatures could predict if the person belonged to the SI-group or not SI-group, as well as discriminate those with SI with history SA from those with SI with no history of SA (Just et al., 2017), it remains to find out if the neural signatures can predict the attempt ahead of the occasion (Auerbach et al., 2020; Just et al., 2017).

### 2.1.5.2 *The HPA-axis*

Self-harming behavior is often associated with stress or a sense of being in a stressful situation. The Hypothalamic-Pituitary-Adrenal (HPA) axis is involved in regulating the body's responses to stress. Studies of the HPA-axis and self-harm has shown differences in the regulation pattern of the HPA-axis among self-harming adolescents, for example lower levels of cortisol after a social stress test (Kaess et al., 2012). Acute pain among individuals with NSSI has been shown to induce increased levels of cortisol and a prolonged automatic arousal as compared to controls (Koenig et al., 2017). Greater autonomic arousal and cortisol

secretion after acute pain/self-injury could help promote stress relief and counteract dissociative states (Koenig et al., 2017). This could at least partly explain the association between childhood maltreatment (blunted cortisol levels; Kalmakis, Meyer, Chiodo, & Leung, 2015) and self-harm, however, further studies are needed (Rinnewitz et al., 2018).

#### *2.1.5.3 Genetic factors*

Genetic studies on self-harm among adolescents are sparse. However, an association between genetic risk and stressful environment has been found (Hankin, Barrocas, Young, Haberstick, & Smolen, 2015). In adult samples an overlap in genetic factors between NSSI and SI, as well as between SI and SA has been found (Campos et al., 2020; Maciejewski et al., 2014).

#### *2.1.5.4 Pain regulation and pain tolerance*

In a review on pain and self-harm, there was strong evidence for an increased pain tolerance among NSSI patients and some evidence for this among suicidal patients. However, the study population consisted mainly of adults (Kirtley, O'Carroll, & O'Connor, 2016). Among adolescents with self-harming behavior, research on the experience of pain have given inconsistent results. Some studies have shown a higher pain threshold and longer pain endurance in self-harming adolescents (Glenn, Michel, Franklin, Hooley, & Nock, 2014; Koenig et al., 2017); yet, another study found no differences in pain threshold between patients with NSSI and matched controls aged 16-24 years (Osuch, Ford, Wrath, Bartha, & Neufeld, 2014). The NSSI-group reported greater relief than the control group after self-administered pain (Osuch et al., 2014). It is likely that the effect of pain in NSSI serves several functions. A study found that among adolescents with NSSI, painful stimulation was found to increase mood and body awareness, while it decreased in controls (Koenig et al., 2017). In young adults, self-criticism has been found to moderate emotional response to pain, i.e. improved mood during pain (Fox, O'Sullivan, Wang, & Hooley, 2019), and in adolescents, a self-critical style was found to mediate the association between NSSI and higher pain threshold (Glenn et al., 2014).

Endogenous opioids are involved in the regulation of affect, pain and reward. Based on a review of endogenous opioids studies and NSSI, it has been proposed that individuals with NSSI have lower baseline levels of endogenous opioids, and that NSSI releases endogenous opioids, which by binding to certain opioid receptors, lead to a reduction in negative affect and possibly an increase in positive affect (Bresin & Gordon, 2013).

## **2.2 COURSE AND OUTCOME**

### **2.2.1 Natural course of self-harm**

Self-harm onset usually occurs in early adolescence, around 12–14 years of age (Cipriano, Cella, & Cotrufo, 2017; Gillies et al., 2018; Nock, 2010). It seems to peak around age 15–17, and declines in young to middle adulthood (Gillies et al., 2018; Moran et al., 2012; Plener et al., 2015; Swannell, Martin, Page, Hasking, & St John, 2014). A study on the natural course of self-harm found self-harm in adolescence to be independently associated with symptoms of depression, anxiety, antisocial behavior, high-risk alcohol use, cannabis use and cigarette smoking. Moreover, symptoms of anxiety and depression during adolescence were predictive of incident self-harm in young adults (Moran et al., 2012). Females seem to continue self-harming to a larger extent than males (Moran et al., 2012).

### **2.2.2 Subsequent outcomes after self-harm**

The physical health and life expectancy have been found to be compromised among individuals who self-harm (Bergen et al., 2012; Moran et al., 2015). Self-harm has been shown to be an independent risk factor for suicide death in two separate meta-analyses (Castellvi et al., 2017; Ribeiro et al., 2016). However, the association between self-harm and suicide death varied considerable across the two studies, OR 1.5 vs OR 22.53 (Castellvi et al., 2017). In young people, between 25-50% of those committing suicide have a previous history of self-harm (Hawton & James, 2005), often self-cutting (Fortune, Stewart, Yadav, & Hawton, 2007; Hawton, Bergen, et al., 2012; Rodway et al., 2016). Studies have found that persons who have been in inpatient care due to self-cutting (Beckman et al., 2018; Carroll et al., 2016; Hawton, Bergen, et al., 2012) or use of violent methods of self-harm (Beckman et al., 2018) are at higher risks of suicide compared with those self-poisoning. Early onset of NSSI (Muehlenkamp, Xhunga, & Brausch, 2019), as well as NSSI frequency have been found to associated and predictive of suicidal behaviors (Gillies et al., 2018; Nock et al., 2006; Victor & Klonsky, 2014; Whitlock et al., 2013), and self-cutting is associated with the highest risk of self-harm repetition when compared to other methods (Bennardi, McMahon, Corcoran, Griffin, & Arensman, 2016; Cully et al., 2019; Hawton, Bergen, et al., 2012). Yet, results are inconsistent, and a population-based cohort did not found method or frequency to be predictive of suicide attempt. Instead, the strongest predictors of transition from NSSI to suicide attempt were drug use and sleep problems (Mars et al., 2019a). Joiner proposed that the act of self-injury could increase the capability of committing suicide by overcoming the fear of pain and hurting oneself (Joiner, 2007). On basis of a review of the literature

concerning the links between non-suicidal self-injury and suicidal behavior, Hamza et al (2012) proposed an integrated model where in addition to the theory of acquired capability (Joiner, 2007), there might be a direct link between NSSI and suicidal behavior, stronger in individuals expiring high levels of psychological distress, and furthermore that there are shared risk factors that explain their high co-occurrence.

Although suicide is the most severe outcome, self-harming behaviors are also associated with other risks regarding subsequent health and well-being. Self-harm in adolescence is associated with increased risks of later substance use (Beckman, Lysell, Haglund, & Dahlin, 2019; Borschmann et al., 2017; Fergusson, Horwood, Ridder, & Beautrais, 2005; Mars, Heron, Crane, Hawton, Lewis, et al., 2014; Moran et al., 2015; Sahlin et al., 2017), violent criminality (Sahlin et al., 2017) and poorer educational (Mars, Heron, Crane, Hawton, Lewis, et al., 2014) and employment outcomes (Beckman et al., 2019; Mars, Heron, Crane, Hawton, Lewis, et al., 2014). When comparing outcomes between individuals with NSSI and those with suicide attempts in a population-based cohort, both groups were found to be at risk of adverse outcomes, but those with suicide attempts were generally at greater risk (Mars, Heron, Crane, Hawton, Lewis, et al., 2014).

With the exception of a large multi-center study from England (Hawton, Bergen, et al., 2012), most longitudinal studies of clinical populations are of small samples (Plener et al., 2015). There is a need for longitudinal studies examining differences in outcomes between NSSI and suicide attempts (Gillies et al., 2018).

#### *2.2.2.1 Sex differences in outcome*

Studies on sex differences in long-term outcomes is sparse. Females with suicidal behavior in adolescence have been found to be at higher risk of developing substance use disorder, while this association was not found among males (Fergusson et al., 2005), and self-harm was a stronger predictor of violent crime among females (Sahlin et al., 2017). No major differences in rates of self-harm repetition have been found between males and females (Bennardi et al., 2016). In general, suicide attempts are more common among women, while committing suicide are more common among males (Hamza et al., 2012; Moscicki, 1994). Studies have shown inconsistent results concerning sex differences in the association between self-harm and suicidal behavior (Andover, Primack, Gibb, & Pepper, 2010; Guan, Fox, & Prinstein, 2012; Victor et al., 2018; You & Lin, 2015). Some studies show no sex differences in the association between NSSI and suicidal ideation or attempts (Andover et al., 2010; Guan et al., 2012), while other find the association between NSSI and suicide attempts to be stronger

among females (Victor et al., 2018; You & Lin, 2015). Within a large register study, hospitalization due to intentional self-harm (between age 10 – 20) was associated with the same risk for death by suicide in both sexes (Beckman et al., 2019). Comparisons between the sexes regarding outcomes can be difficult to interpret, since just being a male or a female affect the risk of the outcomes, rather a comparison within each sex could help us better understand what risks self-harm pose upon males versus females, and whether their risk profiles differs.

### **2.2.3 Borderline Personality Disorder**

Self-harm is one of the criteria for borderline personality disorder (BPD). There is consensus regarding the fact that BPD onset usually occurs in adolescence (Fonagy et al., 2015; Stepp, Lazarus, & Byrd, 2016), and BPD is considered a reliable and valid diagnosis in adolescence (Chanen & McCutcheon, 2013; Fonagy et al., 2015; M. Kaess et al., 2014). However, there is a reluctance among clinicians to diagnose BPD before age 18 (Kaess et al., 2014), and prevalence data on BPD in adolescence is sparse. Prevalence in clinical settings has been estimated to 11% among adolescent outpatients (Chanen et al., 2004) and up to 50% in inpatient settings (Kaess et al., 2014).

#### *2.2.3.1 Borderline Personality Disorder: risk factors and course*

Genetic and environmental factors seem to interact in a neurobehavioral model of the development of BPD (Lieb, Zanarini, Schmahl, Linehan, & Bohus, 2004; Skodol et al., 2002). A twin study showed that BPD traits are heritable, and especially the stability and change of BPD traits over time were highly influenced by genetic factors (Bornovalova, Hicks, Iacono, & McGue, 2009). Marsha Linehan's biosocial model of the development of BPD suggest that the combination of emotional vulnerability (biological factors) combined with an invalidating environment lead to emotional dysregulation and BPD (Linehan, 1993b). Emotion dysregulation is identified as one of the primary mechanisms underlying BPD (Gratz, Moore, & Tull, 2016).

A systematic review of studies examining the risk factors associated with subsequent BPD, found multiple factors associated with BPD, but no disorder-specific factors (Stepp et al., 2016). Individuals who have engaged in both NSSI and suicide attempts (Muehlenkamp, Ertelt, Miller, & Claes, 2011), together with substance misuse (Nakar et al., 2016), seem to be more likely to develop BPD than those with neither NSSI nor suicide attempts (Muehlenkamp et al., 2011; Nakar et al., 2016). BPD is predictive of long-term psychosocial

difficulties even after remission of the disorder (Winograd, Cohen, & Chen, 2008; Zanarini, Frankenburg, Reich, & Fitzmaurice, 2012; Zanarini, Temes, Frankenburg, Reich, & Fitzmaurice, 2018), and BPD is associated with a high mortality rate (nearly 10 % commit suicide). With this in mind, treatment during adolescence is paramount (Bornovalova et al., 2009; Chanen & McCutcheon, 2013; Winograd et al., 2008; Winsper et al., 2015).

## **2.3 TREATMENT OF SELF-HARM AND BORDERLINE PERSONALITY DISORDER IN ADOLESCENTS**

### **2.3.1 Pharmacological treatment**

There are no specific pharmacological treatments available for self-harm or BPD in adolescents, and a lack of RCTs testing pharmacological interventions (Biskin, 2013; Hawton, Witt, Taylor Salisbury, Arensman, Gunnell, Townsend, et al., 2015). A Cochrane review on treatment for self-harm in adults, found no treatment effect for any tested drug but one; in a small single trial flupenthixol (antipsychotic) was found to reduce self-harm, yet, no conclusions were made due to low quality of available evidence and a need for further research (Hawton, Witt, Taylor Salisbury, Arensman, Gunnell, Hazell, et al., 2015). Yet, pharmacological treatments of co-morbid disorders can be helpful (Gunderson et al., 2003). New drugs are being tested for BPD. Oxytocin has shown promising results in some studies; however, more research has been called for (Bertsch & Herpertz, 2018; Herpertz, Schneider, Schmahl, & Bertsch, 2018).

### **2.3.2 Psychological treatment**

#### *2.3.2.1 Treatment of self-harm in youth*

Psychosocial therapy interventions after self-harm lower the risk of repeated self-harm (Erlangsen et al., 2015; Glenn, Esposito, Porter, & Robinson, 2019; Kothgassner, Robinson, Goreis, Ougrin, & Plener, 2020) and death by any cause both in short-term and long-term follow-up, and lower the risk of subsequent suicide, especially among children and adolescents (age 10-24) (Erlangsen et al., 2015). Systematic reviews and meta-analyses have shown that interventions with treatment elements such as parent training/education, skills training, and sufficient dose of treatment were associated with positive outcomes in adolescents with self-harming behaviors (Brent, 2019; Brent et al., 2013; Glenn, Kleiman, et al., 2019; Ougrin, Tranah, Stahl, Moran, & Asarnow, 2015). In a recent systematic review including 26 RCTs on treatment for self-injurious thoughts and behaviors in youth, dialectical behavior therapy for adolescents (DBT-A) met the criteria for a well-established

intervention (i.e. efficacy demonstrated in two independent RCTs) for reducing deliberate self-harm (Glenn, Esposito, et al., 2019). Five other interventions were rated as probably efficacious, showing promising results in single trials (Glenn, Esposito, et al., 2019). A meta-analysis of 25 RCTs ( $N = 2962$ ) on interventions for self-harm and suicidal ideation in adolescents found greater decrease of self-harm, suicidal ideation and depressive symptoms for the therapeutic interventions as compared with the control condition (TAU, EUC), although with a small effect sizes ( $d = 0.13$ ,  $d = 0.31$ , and  $d = 0.22$  respectively) (Kothgassner et al., 2020). Moreover, it was found that the control conditions showed medium to large effect sizes in reducing self-harm, suicidal ideation and depressive symptoms in pre-to-post interventions. Only DBT-A showed significantly better outcomes in reducing self-harm as compared to control condition, while both DBT-A and family-centered therapy showed effect in reducing suicidal ideation (the latter with large heterogeneity in the results)(Kothgassner et al., 2020). There is a need for independent replication studies of interventions with promising results, as well as studies on core components in treatment for development of brief interventions, easily accessible to a large number of youth (Glenn, Esposito, et al., 2019; Kothgassner et al., 2020). Also, since most research has been conducted on self-harming women, the question arises whether assessment and treatment strategies need to be different for males (Laye-Gindhu & Schonert-Reichl, 2005; McCauley et al., 2018; Monto et al., 2018; Victor et al., 2018; Wilkinson, 2018). It has been pointed out that there is a need for better understanding of the key outcomes from the patient's perspective (Little, Tickle, & das Nair, 2018). Quantitative studies usually utilize changes in NSSI, suicide attempts and suicidal ideations as primary outcomes, however, these are not necessarily the key outcomes for the patients (Little et al., 2018).

It is acknowledged that self-harming patients often have negative experiences of health care services (Statens beredning för medicinsk och social utvärdering [SBU], 2015; Eriksson & Åkerman, 2012; Law, Rostill-Brookes, & Goodman, 2009; Taylor, Hawton, Fortune, & Kapur, 2009), which might, at least partly, be explained by negative attitudes among health professionals towards self-harming patients (Saunders, Hawton, Fortune, & Farrell, 2012). Specific training in the management of self-harm has been found to increase knowledge and improve attitudes among health professionals (Saunders et al., 2012). In a meta-analysis including 39,131 adolescents from community-based samples, 48% was found to seek help or tell someone about their self-harm, most commonly a friend, and, as the authors argue, there might be a need of aid for the young person asked to help a friend who self-harms (Gillies et al., 2018).

### *2.3.2.2 Treatment of BPD in youth*

The BPD traits, such as emotional instability, explosive anger and impulsivity, in youth are suggested to be flexible and malleable, and early interventions are thought to be gainful (Bornovalova et al., 2009; Chanen et al., 2008; Chanen & McCutcheon, 2013; Kaess et al., 2014; Lenzenweger & Castro, 2005). However, high quality trials for treatments on youths with BPD are sparse (Biskin, 2013). Neither mentalization-based treatment in group (MBT-G), a one-year intervention with three components; introduction (psychoeducation about BPD, attachment and mentalizing), weekly group sessions and parent psychoeducation and training (Beck et al., 2020) nor Emotion Regulation Training (ERT), a 17-session weekly group training in addition to TAU (Schuppert et al., 2012), were in RCTs found to be superior to TAU in reducing BPD features in adolescents (Beck et al., 2020; Schuppert et al., 2012). There are no specific risk factors for developing BPD; however targeting groups with signs and symptoms for indicated prevention are thought to be feasible (Chanen et al., 2008; Kaess et al., 2014). The Helping Young People Early (HYPE) clinic, is developed to provide both indicated prevention and early intervention for BPD in youth (Chanen, McCutcheon, et al., 2009). Within the HYPE program Cognitive Analytic Therapy (CAT) is given. In an RCT, HYPE + CAT was compared to HYPE + good clinical care (GCC; structured high-quality care). Although those who participated in HYPE + CAT showed a more rapid recovery, the 2-year outcome was similar (Chanen et al., 2008). In a quasi-experimental study comparing HYPE + CAT, HYPE + GCC to treatment as usual (the treatment given prior to the implementation of HYPE), the most effective intervention was HYPE + CAT (Chanen, Jackson, et al., 2009). In pipeline is an RCT aiming at evaluating the effect of adding a model for vocational support (Individual Placement and Support) to the HYPE program (Chanen et al., 2020). Increased knowledge of efficient methods to increase vocational functioning is needed. Adolescent symptoms of BPD predict vocational impairment in adulthood (Winograd et al., 2008), and vocational impairment has been found to be a leading reason for not achieving or maintaining recovery in BPD (Temes & Zanarini, 2018)

### *2.3.2.3 Mentalization-based treatment for adolescents*

Mentalization-based treatment for adolescents (MBT-A) is a modified version of mentalization based therapy (MBT), for depressed adolescents with self-harming behavior (Rossouw & Fonagy, 2012). MBT aims to improve the BPD patient's capability to mentalize (Bateman & Fonagy, 2013). One RCT on MBT-A treatment of self-harm in adolescents (85% girls, 73 % meeting criteria for BPD), showed a greater reduction in self-harm after 12 months of treatment, however with large dropout rates (Rossouw & Fonagy, 2012).



#### *2.3.2.4 Cognitive behavioral therapy for self-harm*

Different forms of cognitive behavioral therapy (CBT) for treatment of self-harm have been tested in RCTs. Single RCTs have found that a 12-week family-based CBT-treatment led to reduced risk of suicide attempts as compared with enhanced treatment as usual (Asarnow, Hughes, Babeva, & Sugar, 2017), another CBT intervention with family components (Integrated CBT, I-CBT) resulted in fewer suicide attempts as compared with usual care (Esposito-Smythers, Spirito, Kahler, Hunt, & Monti, 2011), yet within a subsequent larger trial with a modified version of I-CBT, i.e. family-focused cognitive behavioral therapy (F-CBT), within a sample with more severe symptom, F-CBT was not found to be more efficient than enhanced care (Esposito-Smythers et al., 2019). Similarly, a brief CBT intervention, the "Cutting Down Program" (CDP; 8–12 sessions), had promising result in a previous pilot study (Taylor et al., 2011), however, in a subsequent RCT, CDP was not found to be superior to TAU in reducing NSSI frequency, however, in the CDP group reductions in NSSI frequency was reached faster and with fewer treatment sessions (Kaess et al., 2020).

#### *2.3.2.5 Dialectical behavior therapy for adolescent*

DBT-A is an adapted version of Marsha Linehan's DBT, a treatment developed for self-harming adults with BPD (Linehan, 1993b; Miller, 2007; Rathus & Miller, 2002). DBT is based on behavioral sciences, dialectical philosophy and Zen Buddhism (Linehan, 1993a), and involves the following components: individual therapy, group skills training, phone coaching and therapist consultation team. In the adolescent version, treatment length has been decreased, family-members/care-givers are included in treatment (parent/multi-family skills training groups, family sessions etc.), adaptations of the skills have been made (e.g., adding a new skill module), and age-appropriate terminology is used (Klein & Miller, 2011). In a recent Cochrane review on psychological therapies for BPD, mean age ranging between 14.8–45.7 years, DBT was more effective than TAU in reducing BPD severity, although, based on evidence with low-quality (Storebø et al., 2020). Uncontrolled studies targeting BPD traits in adolescents have shown promising results for DBT-A (Buerger et al., 2018; M. Kaess et al., 2014; MacPherson, Cheavens, & Fristad, 2013). However, with no control group it is difficult to state that this was due to the specific treatment.

DBT-A has the strongest empirical support for treatment of self-harm in adolescents, with two independent RCTs showing reduction in self-harm with treatment (McCauley et al., 2018; Mehlum et al., 2019). At a 3-year follow up, DBT still was superior in reducing self-harm, however no differences between DBT and enhanced usual care was found regarding

suicidal ideation, hopelessness, borderline and depressive symptoms (Mehlum et al., 2019). Attempts have been made to identify which core components of DBT, and mediators or moderators, that may be crucial for positive outcomes. DBT skills have been shown to mediate decrease in NSSI and suicide attempts (Barnicot, Gonzalez, McCabe, & Priebe, 2016; Neacsiu, Rizvi, & Linehan, 2010), yet standalone DBT skills training group, or combined with case management, has not been found to be as efficient as standard DBT (Linehan et al., 2015; Lyng et al., 2020). Reductions in perceived hopelessness mediated 70.8% of the effect of DBT on self-harm frequency at a 3-year follow up (Mehlum et al., 2019). Furthermore, DBT has been found to be most beneficial for adolescents with high levels of baseline emotional dysregulation, whose parents had high levels of psychopathology (Adrian et al., 2019). From the patient's perspective on DBT, the relationship with the therapist has been highlighted (Little et al., 2018), as well as patient herself taking responsibility for treatment, a change in perspectives and mastering skills and language of DBT (Lakeman & Emeleus, 2020; Little et al., 2018).

Clinical studies tend to maximize the internal validity, but attenuate the external validity and hence limits the generalizability of the studies (Weisz, Weiss, & Donenberg, 1992; Wells, 1999; Wilkinson, 2018), for example; with strict inclusion and exclusion criteria in selected settings. Also, detected statistically significant treatment effects are not necessarily clinically significant, e.g. the effect might be too small to make any explicit clinical difference for the patient (Jacobson & Truax, 1991). The feasibility and effectiveness of DBT with suicidal and self-harming adolescents in a community mental health setting was tested with a small sample in an open trial, showing statistically significant pre-post treatment decreases in suicide attempts, NSSI and suicidal ideation (Berk, Starace, Black, & Avina, 2018). Further studies of the utility of the treatment in larger adolescent samples in natural settings, as well as studies on long-term outcomes after DBT in adolescence, are needed. Also, DBT is a resource-intensive treatment and there is a need for more easily accessible interventions (Gillies et al., 2018), studies exploring the adolescent's experience of which components of DBT that are particularly helpful or meaningful, could guide the development of such interventions.

### 3 AIMS OF THE THESIS

The overall aim of the thesis was to study the clinical presentation, subsequent outcomes and experiences of DBT among boys and girls who seek help for self-harming behaviors within the CAMHS in the Stockholm County. The specific aims and research questions addressed in the individual studies were as follows:

**Study I:**     **Aim:** To compare clinical and psychosocial correlates as well as subsequent adverse outcomes among three groups of youths who present to the CAMHS, those with: 1) self-harm without suicidal ideation/behavior, 2) self-harm and suicidal ideation/behavior, 3) clinical controls with no documented self-harm or suicidal ideation/behavior.

**Research question:** Do help-seeking adolescents with self-harm—with or without suicidality—display a higher problem load and subsequent more adverse outcomes compared to clinical controls?

**Study II:**   **Aim:** To examine subsequent adverse outcomes (alcohol/substance misuse, psychiatric inpatient care, criminality, and suicide) associated with care contact due to self-harm during adolescence, in a large enough sample to explore sex differences.

**Research question:** Do help-seeking boys and girls with self-harming behaviors in adolescence differ with regard to outcomes?

**Study III:**   **Aim:** To examine adverse clinical outcomes among a sample of adolescents who had previously been assessed as displaying NSSI or SA, while including NSSI and SA as time-varying covariates.

**Research question:** Do adolescence with NSSI or SA differ in adverse clinical outcomes compared to clinical controls?

**Study IV:**   **Objective:** To explore how former DBT-A patients experienced DBT, and specifically if there were aspects of the treatment that emerged as particularly meaningful or helpful, or unhelpful and perhaps harmful.

**Research question:** What makes treatment efficacious from the patient's perspective?



## 4 MATERIAL AND METHODS

### 4.1 DATA SOURCES

#### 4.1.1 Participants

Included participants in all four studies in this thesis were former or present patients at the public Child and Adolescent Mental Health Services (CAMHS) in Stockholm County (a metropolitan area with more than 2 million inhabitants). The CAMHS provide specialist level psychiatric out- and inpatient care for inhabitants below the age of 18. There are a few private caregivers commissioned by the County Council, but the public CAMHS holds about 90% of the care budget. During 2019, 5.1 % of all inhabitants age 0–17 in the county ( $N \approx 520,000$ ) had been in contact with either the public or private CAMHS; of these 54 % were boys and 46 % girls, although, the girls had somewhat more visits. More than half of the girls (58%) were between age 13–17, while the boys tended to be of a younger age (40 % age 7–12, 48 %, age 13–15). The vast majority of contacts were outpatient visits and the most common contact reasons at the outpatient services were anxiety or ADHD related problems. Only 0.001% of all inhabitants age 0–17 had received inpatient care. Median inpatient stay were 10.5 days (Uppdrag Psykisk Hälsa, 2020). This is a snapshot of the care statistics at CAMHS, and the distributions in terms of ages (accordingly also sex and contact reasons) shift across time due to underlying demographic factors.

In study I, the cross-sectional cohort included all individuals between ages of 4 and 18 years who had been in contact with the CAMHS between 2011 and 2015 ( $N = 25,161$ , 46% girls), and the longitudinal cohort included all individuals who had terminated their contact with the CAMHS between 2011 and 2015, and were born before December 31 1997 ( $N = 6,120$ , 50% girls). Study II included all patients enrolled at CAMHS between 2001 and 2015 ( $N = 110,072$ , 49% girls). Study III included all individuals between ages of 5 and 17 years enrolled at CAMHS between December 2011 and December 2013 ( $N = 17,192$ , 48.6% girls). Study IV included all individuals who had received DBT-A ( $\geq 40$  visits at the DBT-unit) between 2006 and 2015, and were  $\geq 18$  years of age at time of study interview ( $N = 251$ , 96% girls). See figure 3.

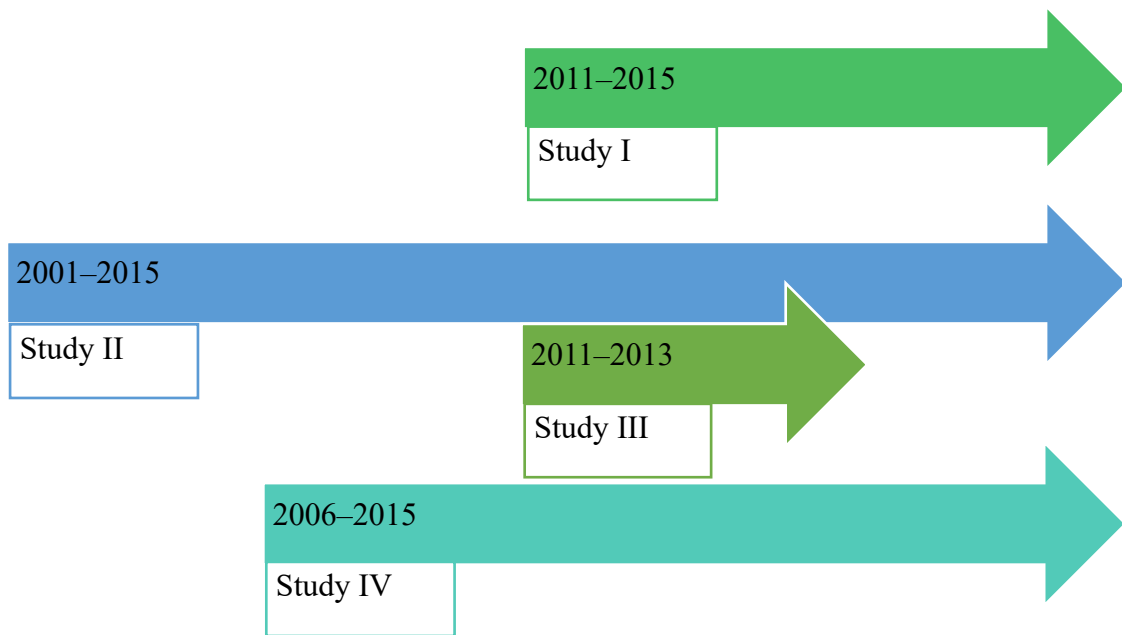


Figure 3: Illustration of the different time spans for participant inclusion used in studies I to IV.

#### 4.1.2 The Pastill Register

The Pastill Register is a regional, clinical register holding information on all individuals seeking care at the public CAMHS. The Pastill Register was introduced in 1999, and since 2001, the register holds complete data on each patient's contact reasons, treatment provided, mental disorders according to the ICD-10, psychotropic medication, psychosocial problems, and global functioning. Data on NSSI and suicide attempts as contact reasons are available since 2011, but prior to that date no differentiation between NSSI and suicide attempts were made. A mandatory registration is made in the Pastill at patient intake and treatment termination as part of the clinical routine. Data on contact reason and psychosocial problems are manually documented by the clinician, while the remaining data are derived directly from the digital charts. The Pastill Register was used in study I to III.

#### 4.1.3 Swedish National Registers

All Swedish citizens are at birth or when obtaining citizenship, assigned a unique personal identification number. By this identification number, data on each individual are held in different national registers kept by Statistics Sweden. Data from the Pastill Register are linked to the National Registers by the personal identification number, figure IV. The National Registers used in study I to III are:

- The National Patient Register (NPR): holds information on all psychiatric inpatient care from 1973, and psychiatric outpatient care since 2001, including diagnosis codes according to the World Health Organization's International Classification of Diseases (ICD), since 1997 according to ICD-10 (World Health, 1992).
- The Swedish Prescribed Drug Register: holds information on all prescribed and dispensed drugs (i.e. Anatomical Therapeutic Chemical classifications system [ATC] code, drug name, strength, pack size) in Sweden and was established in 2005. The data is updated on a monthly basis. It does not include drugs administered at hospital or nursing homes, or vaccines (Socialstyrelsen, 2020).
- The National Crime Register: holds data on all criminal (non-violent and violent) convictions in Swedish lower courts.
- The Register of Persons Suspected of Offences: have data on suspicion of a crime after complete investigation by police or other authority.
- The Multi-Generation Register: holds information on family relations, e.g. linkage between the index person and the biological parents or adoptive parents.
- The Longitudinal Integration Database for Health Insurance and Labor Market Studies (LISA): holds data on education, employment, health insurance, parental insurance and unemployment insurance for each person age  $\geq 16$ , and since 2010 from age  $\geq 15$ . Data are available from 1990 and are updated yearly.
- The Cause of Death Register: holds information on all deaths and the registered cause of death. Updated yearly.

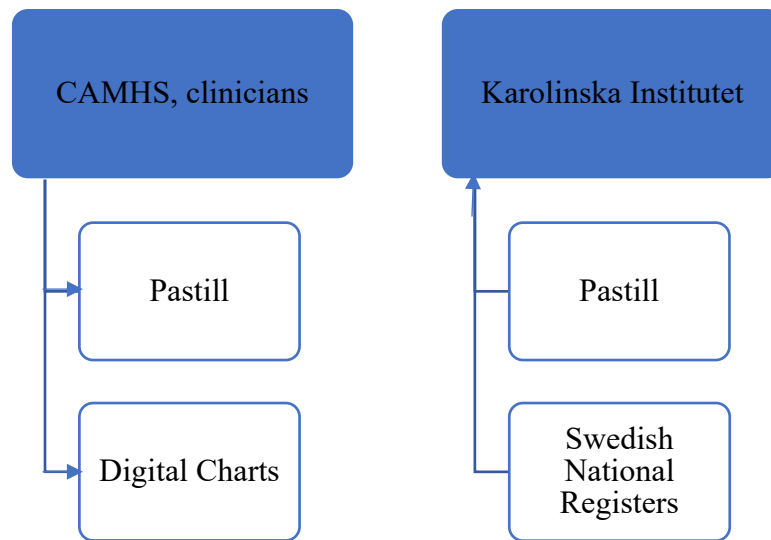


Figure 4: Data are documented in the Pastill either directly by the clinician or derived from the digital charts. The Karolinska Institutet holds data from the Pastill register linked to Swedish National Registers.

#### 4.1.4 Definition of cases and controls

In the case-control study (study I) cases were defined as: (a) having self-harm (SH) without any indication of suicidal ideation or behaviors (SU), or (b) having at least one SH and at least one SU as contact reason in the Pastill Register. Controls were all patients who had been in contact with CAMHS for other reasons than SH or SU.

#### 4.1.5 Exposures

In longitudinal cohort studies (study I to III) exposure was defined as: (a) having SH without any indication of SU (study I), (b) or at least one SH and at least one SU (study I), (c) or self-harm with unknown intent (study II), or (d) NSSI or SA, assigned as one (of potentially several) contact reason(s) in the Pastill Register.



## 4.2 MEASURES

### 4.2.1 Clinical and psychosocial correlates

#### 4.2.1.1 *Clinical care consumption*

Clinical care consumption was measured as the total number of outpatient visits, number of psychiatric admissions, and number of nights in inpatient care, as registered in the Pastill register.

#### 4.2.1.2 *Global functioning*

The Children's Global Assessment Scale (C-GAS; Shaffer et al., 1983) is used within the CAMHS units for ratings of global functioning. C-GAS ranges from 0 to 100, higher scores equal better functioning. The scale has shown moderate to excellent interrater reliability and stability over time (Shaffer et al., 1983). A Swedish study found moderate interrater reliability among C-GAS raters using the Pastill Register (Lundh, Kowalski, Sundberg, Gumpert, & Landen, 2010). Registration of global functioning, as a value on the C-GAS, is mandatory at the initiation and the termination of contact within the CAMHS.

#### 4.2.1.3 *Mental disorders*

Diagnosis of mental disorder was measured as a record of an ICD-10 diagnosis at any time between 2011–2015, the following ICD-10 codes were included; alcohol use disorders, F10; substance use disorders, F11–19; psychotic disorders, F20–29, F323; depressive disorders, F30–34; anxiety disorders F40–43; eating disorders, F50; Attention-deficit hyperactivity disorders (ADHD), F90; and autism spectrum disorders, F84.

#### 4.2.1.4 *Prescribed psychotropics*

From the Prescribed Drug Register prescription of antidepressants, sedatives and hypnotics according to the ATC codes N06A (antidepressants) and N05C (sedatives and hypnotics), were used for calculating the odds of being prescribed these medications in comparison to the clinical controls.

#### 4.2.1.5 *Psychosocial problems*

At patient intake and termination, registration of the presence of psychosocial problems is done in the Pastill Register. The following areas are covered: problems in relationship within the family, psychological problems in the family, familial violence, and problems with

friends. The registrations are a mandatory part of the clinical routine. These registrations were used to measure psychosocial correlates.

## **4.2.2 Longitudinal outcomes**

### *4.2.2.1 Alcohol and/or substance use disorder*

The outcome measure for alcohol and or substance use disorder was any record in the NPR of the ICD-10 codes F10–19.

### *4.2.2.2 Self-harm*

The outcome measure for subsequent self-harm was any record in the NPR of intentional self-harm, ICD-10 codes X60–84; or one or more event of undetermined intent, ICD-10 codes Y10–34.

### *4.2.2.3 Suicide*

Information on suicide was collected from the Cause of Death Register.

### *4.2.2.4 Inpatient care*

The outcome measure included all psychiatric inpatient care related to ICD-10 codes F20–90, as registered in the NPR.

### *4.2.2.5 Use of psychotropics*

The outcome measure was dispensed psychotropic medication, i.e. ATC code N05C (hypnotics and sedatives) and ATC code N05B (anxiolytics), according to the Prescribed Drug Register.

### *4.2.2.6 Recipience of social welfare*

Information on recipiency of social welfare was collected from the LISA.

### *4.2.2.7 Criminality*

The outcome measure for criminality (non-violent or violent) was defined as either being convicted or suspected for non-violent or violent crime within the National Crime Register or the Register of Persons Suspected of Offence.

## **4.3 STUDY DESIGNS**

### **4.3.1 Case-control study**

In study I, we conducted a case-control study, which is an observational study design. In case-control studies the sampling begins with the cases (in this case, those with self-harm), which are compared with the controls that do not have the case-status but are at risk of contracting the case-status. Case-control design are useful for studies on several exposures (as in study I) and rare outcomes, but are less suitable for studying rare exposures and several outcomes. Case-control studies are often retrospective but can also be prospective. The outcome measures in case-control studies are OR (Rothman, 2012). Since we aimed to examine whether patients with self-harm were at higher or lower odds of having a variety of clinical and psychosocial correlates as compared with patients with no self-harm, a case-control design was chosen. Case-control studies are susceptible for biases, and in particular selection bias. We included everyone with the exposure of interest (i.e. self-harm) but most likely there are unidentified cases among our controls, since self-harm is not always disclosed.

### **4.3.2 Cohort study**

In study I, II, and III we conducted cohort studies. A cohort study is a longitudinal study, with an analytical, observational study design. Cohort studies are used for measurements of outcomes after exposures. Cohort studies are particularly useful for studying several outcomes, as well as several exposures or rare exposures. The cohorts are selected from a population, and the individuals in the cohort shall be at risk of the outcome, but may not have the outcome at baseline, and are followed over time. Cohort studies can be prospective or retrospective. Outcomes within exposed versus unexposed individuals are measured, and risk or rate of an incidence can be calculated and reported (Rothman, 2012, p. 84). However, the chosen statistical analysis might only report ratios, as is the case in the Cox regression model (See 4.4.3), a commonly utilized method within medical research. As we aimed to compare several outcomes between different exposures within a clinical population, a cohort study design was applied in study I to III.

### **4.3.3 Qualitative approach**

In qualitative studies, knowledge is viewed and achieved differently than in quantitative research. Rather than testing hypotheses and providing results that hold statistical significance, qualitative research aims at for example capturing the experience or view of the

individual, or at developing an understanding of a phenomenon. Qualitative studies can produce hypotheses that may later be tested in quantitative designs (Bradshaw, Atkinson, & Doody, 2017; Malterud, 2001a, 2001b).

#### *4.3.3.1 Reflexive thematic analysis*

Study IV is a qualitative study, and a reflexive thematic analysis was conducted to analyze data from interviews. Reflexive thematic analysis offers a flexible tool (in terms of underlying theory, inductive/deductive proceeding, latent or semantic coding) for analysis. It is a relatively easily accessible method for researchers with limited experience of qualitative research (Braun & Clarke, 2006), however it is essential for the researcher to understand and express which theoretical assumptions that are held, and how knowledge is reached within this theoretical framework (Braun & Clarke, 2019).

### **4.4 STATISTICAL ANALYSES**

Regression models are useful for studying the effect of independent variable/variables (exposure) on the dependent variable (outcome). There are many different regression models, below I will describe the three models utilized in study I to III.

#### **4.4.1 Linear regression**

The linear regression model uses the mathematical equation for the straight line ( $y = mx + c$ , where  $m$  is the coefficient/slope of  $x$ , and  $c$  is the intercept) for describing the relationship between the independent and dependent variable. The model makes four main assumptions: there is a linear relationship between the independent and dependent variables; the observations are independent of each other; the residuals are normally distributed; and have a constant variance (homoscedasticity). The coefficient/slope is calculated and tested if significant (usually if  $p < 0.05$ , the null hypothesis is rejected). Linear regression is suitable when the dependent variable is continuous, and the independent variables are continuous, binary or categorical (Marill, 2004; Rothman, 2012; Schneider, Hommel, & Blettner, 2010).

Linear regression was utilized in the cross-sectional analysis in study I, for estimating the associations between self-harm and clinical care and global functioning. Since the required assumption of normal distribution was not met, a variance-covariance estimator was used. The variance-covariance estimator allows us to do linear regression and interpret the regression parameters as usual, although the assumptions of normal distribution or homoscedasticity are not met (Pawitan, 2001).

#### **4.4.2 Logistic regression**

When the dependent variable is dichotomous (e.g. yes/no, 0/1), logistic regression can be used. In the logistic model the quantity  $\ln[R/(1-R)]$  ( $R$  = the risk measure) is the dependent variable of the straight-line equation ( $y$ , in the example above, see 4.4.1). By using the logistic transformation, the measures can range from minus infinity to plus infinity, but the outcomes in logistic regressions are expressed as OR, usually with a 95% confidence interval (CI). OR equals the odds of the outcome if exposed divided by the odds of the outcome if unexposed. If the outcome is rare, the OR can be used to calculate risk ratio. The 95% confidence interval express the range within we are 95% confident that the true value of the population is. The assumptions made in logistic regressions are these; it is a random sample, data are not biased, there should be a linear relationship with the independent variable and the log odds, and the sample need to be large (Rothman, 2012; Stoltzfus, 2011).

With OR as outcome measure, logistic regression is useful in case-control studies, and was utilized in the case-control analysis in Study I, for examining the associations between self-harm and mental disorders, psychotropic medication and psychosocial problems.

#### **4.4.3 Cox regression**

In longitudinal studies time is a variable, and survival analysis (e.g. time to event) is performed. There are different regression models for survival analysis, and one of the most commonly used within medical research are Cox regression or Cox proportional hazards regression/model (Bender, 2009). The necessary assumption in Cox regression is that the hazard rates are proportional. When using Cox regression, no measure of the incidence rate is achieved, rather the hazard ratio (HR). The HR estimates the ratio between the hazard of an event in the exposed group and the hazard of an event in the unexposed group (Spruance, Reid, Grace, & Samore, 2004). A disadvantage of the Cox regression model is that it only reports the ratios, not the rate or actual risks. However, since study I to III had relatively short follow up times, and the proportional hazards assumption was not violated, the Cox regression model was estimated to fit for the statistical analysis and provide us with adequate information on differences in outcomes between exposed and unexposed. In study III, time-varying covariates were included in the model (Fisher & Lin, 1999).

### **4.5 ETHICAL CONSIDERATIONS**

All studies in the thesis were conducted in accordance to the Helsinki Declaration (World Medical Association, 2013), and approved by the Stockholm Regional Ethics Committee.

Within all research involving humans, the anticipated gains and importance of a study must outweigh the risks and burdens for the study participants. Furthermore, measures must be made to minimize the risks (World Medical Association, 2013). Below I describe the ethical considerations and precautions that were made with regards to the studies included in the thesis.

#### **4.5.1 Ethics within the register studies**

Large register studies usually do not demand informed consent from the participants, rather the Ethics Committee represent the interests of the study participants, and approval from the Ethics Committee can replace the individual approvals from the participants (Ludvigsson et al., 2015). Register studies usually do not cause the participants any liabilities, but there are still some risks to consider: First, the risk of identification of a participant. In study I to III, the regional care register (Pastill) was linked with national registers by using the personal identification number. The linkage was accomplished by Statistics Sweden, and data was anonymized before handled over to the research group. Thereby, no identification of the study participants was possible. Second, there may be a risk of results being misused or wrongfully interpreted by decision makers or the media. We aimed to prevent this by careful interpretation of the data, and lucid communication of the results.

#### **4.5.2 Ethics within the qualitative study**

The ethical considerations concerned different aspects of interviewing former patients. The study targeted individuals with traits of emotional instability and a history of severe symptoms. Asking questions about experiences during a difficult time of life might trigger an emotional arousal. Precautions were made by making sure the interviewer was percipient and checked the individual both during and after the interview, and the interviews were held in a clinical setting. Another ethical concern was that the study participants themselves would not gain any benefit for participating, else than the possibility to give feedback to former caregivers. However, the utility of studies on young people with self-harming behavior in the society as a whole is large. More efficacious prevention strategies, assessment and treatments are needed. It would be an ethical problem if research could not be done on these patient groups despite challenges. Data were held encoded throughout the whole process and only the interviewer knew the participants' identity.

## 5 STUDY SUMMARIES AND RESULTS

Below I present a brief summary of each of the four studies included in this thesis and their main results. In register studies I to III young patients with self-harm had higher problem loads and were at higher risks of adverse outcomes as compared with controls. Suicidality in addition to self-harm worsened the prognosis. Boys and girls had similar risk profiles with increased risks for adverse outcomes as compared with controls within their same sex. The qualitative analysis in study IV revealed approaches that were helpful in building a working relationship with the therapist, and that meeting peers within skills training groups were an appreciated and essential part of treatment.

### 5.1 STUDY I -SELF-HARM AND SUICIDAL BEHAVIORS, CLINICAL CORRELATES AND OUTCOMES

Study I consists of two separate analyses; one case-control study and one longitudinal cohort study, including data on three separate groups of former patients at CAMHS. The case-control study included all patients, age 4–18 years, that had been in contact with the CAMHS between 1<sup>st</sup> of January 2011 and 31<sup>st</sup> of December 2015. Those with documented self-harm (SH) as contact reason at one or more occasions but no documented suicidal ideation/behavior (SU) comprised one case-group ( $n = 1,027$ ). The second case-group comprised those with both SH and SU ( $n = 1,099$ ). The controls were patients with no documented SH or SU ( $n = 21,119$ ). With the aim to compare clinical and psychosocial correlates between cases and controls, we measured clinical care consumption, global functioning (C-GAS), comorbidity (diagnosis of mental disorder, ICD-10), prescription of antidepressants, sedatives and hypnotics, and clinician-rated psychosocial problems. Two sets of analyses were performed: the SH-cases compared with controls, and the SH + SU cases compared with controls. Linear regression analysis was used for examining associations with clinical care and global functioning. Logistic regression was used to examine associations between case-status and comorbidity, psychotropics, and psychosocial problems, expressed as OR with 95% CI. Adjustments were made for socioeconomic status, age at first CAMHS contact and sex.

The longitudinal cohort ( $N = 6,120$ ) comprised former CAMHS patients who had ended their CAMHS contact between 1<sup>st</sup> of January 2011 and 31<sup>st</sup> of December 2015, and were  $\geq 18$  years of age at 31<sup>st</sup> of December 2015. As in the case-control study, the cohort was divided into the three different groups; SH patients ( $n = 261$ ), SH + SU patients ( $n = 363$ ), and no SH or SU patients ( $n = 4,746$ ). With the aim to compare adverse outcomes between the exposed

(SH or SH + SU) and unexposed (no SH or SU), the cohort was followed up in national registers regarding alcohol/substance use disorder (ICD-10 codes F 10-19), any event of self-harm (intentional, ICD-10 codes X60–84; or undetermined intent, ICD-10 codes Y10–34), completed suicide, psychiatric inpatient care, dispensed psychotropic medication (hypnotics, sedatives, and anxiolytics), reciprocity of social welfare, conviction/suspicion of violent crime, and conviction/suspicion of non-violent crime. Differences in outcome rates between exposed and unexposed were estimated using Cox proportional hazards model for the HR with 95% CI for each outcome. In a supplementary analysis, those presenting with SU only, no SH, were compared with clinical controls on all measures.

### **5.1.1 Results**

Being a patient with SH or SH + SU was associated with greater problem load and higher risks for adverse outcomes compared with patients with no documented SH or SU at the CAMHS. The patients with SH + SU was the most burdened group, with stronger risk associations and more severe outcomes. The patients with SH had on average 7.3, 95% CI [5.3, 9.6], more visits to the CAMHS as compared to clinical controls, yet, patients with SH + SU had on average 30.7, [28.3, 33.1], more visits to the CAMHS. Patients with SH had higher odds than the clinical controls for depressive disorders, anxiety disorders and eating disorders, (OR range 1.8–2.3) while the odds for patients with SH + SU for the same disorders ranged from 3.9–8.7. Also, patients with SH + SU had on average 7.8, [6.8, 9.8] more nights of inpatient care as compared with controls. The longitudinal study had a median follow up time of 2.8 years (Min: 0, Max: 5). The same pattern was found as in the case-control study; both patients with SH and patients with SH + SU were at greater risk of adverse outcomes compared with the unexposed patients, and again the patients with SH + SU had the highest risks and had more severe outcomes. For patients with SH the adjusted HR for recurrent care due to self-harming acts was 3.9, [2.3, 6.7], in patients with SH + SU it was 23.1, [17.0, 31.4]. Similarly, for patients with SH the adjusted HR for inpatient care was 1.7, [1.0, 2.7], while in patients with SH + SU it was 11.3, [8.9, 14.4]. Patients with SH + SU were also at increased risk for social welfare reciprocity (HR = 2.6, [1.6, 4.3]), non-violent crime (HR = 2.1, [1.6, 2.8]) and violent crime (HR = 2.0, [1.3, 3.1]). Results from supplementary analyses found that presenting with SU only was associated with similar levels of burdens and risks for subsequent adverse outcomes as presenting with SH only.



## **5.2 STUDY II -SEX DIFFERENCES IN OUTCOMES AFTER SELF-HARM**

In this longitudinal cohort study, we expanded the cohort of CAMHS patients in order to have a large enough sample to explore sex differences. Therefore, we included patients enrolled at CAMHS between 2001 and 2015 ( $N = 110,072$ ). Since differentiation between SH and SU was only available in the Pastill register from 2011, the chosen exposure this time was self-harm with unknown intent (suicidal or non-suicidal) as contact reason. With the aim to examine subsequent adverse outcomes associated with care contact due to self-harm during adolescence, the cohort was followed for the outcomes in the national registers, from the last registered CAMHS contact until the end of 2015. The outcome measures were alcohol or substance use disorder, inpatient psychiatric care, criminality and suicide. Differences in outcome rates were analyzed between exposed males versus unexposed males, and exposed females versus unexposed females, using Cox regressions and expressed as HR with 95% CI.

### **5.2.1 Results**

The median follow up time was 5.8 years (Q1: 2.3 years; Q3: 9.7 years). Self-harm as contact reason was documented in 2.2% ( $n = 1,241$ ) of all males and in 8.7% ( $n = 4,716$ ) of all females. Both males and females with self-harm had higher HR for all outcomes as compared with unexposed patients of their own sex. For males the HR ranged from 3.2–7.2, with the highest HR for psychiatric inpatient care and the widest 95% CI for suicide, for females the HR ranged from 5.1–9.7, with the highest HR for substance use disorder and the widest 95% CI for suicide. Females with self-harm had a more pronounced risk for drug use disorder (HR = 11.2, 95% CI [9.9, 12.7]) compared with males with self-harm (HR = 6.5, [5.2, 8.0]). Both males and females with self-harm have an elevated risk for future suicide (although large CIs), with a HR for males of 4.7 [1.1, 20.1], and for females 7.8 [3.7, 16.7].

## **5.3 STUDY III -OUTCOMES AFTER NSSI VERSUS SA**

In this longitudinal study, the cohort comprised patients (age 4–18 years) that had sought care at the CAMHS between 2011 and 2013 and had undergone one or several clinician ratings of non-suicidal self-injury (NSSI) and suicide attempts (SA). Although at first sight similar to study I, study III is different in that study I could not differentiate between suicidal ideation and SA, and the exposure (self-harm or suicidal ideation/behavior) was based on a single measure at baseline. In study III we aimed to compare clinical outcomes among adolescents who were rated with NSSI or SA, with adolescents rated with neither NSSI nor SA, and take into account that suicidal intention may vary over time, by using Cox regressions with NSSI and SA as time-varying covariates. Outcome measures were alcohol/substance use disorder,

subsequent episodes of self-harm (ICD-10 diagnosis of X60–84 or Y10–34) and psychiatric inpatient care.

### 5.3.1 Results

Mean follow up time was 7.0 months. Of the 2,219 patients who had undergone NSSI/SA ratings, 34% were assessed as having NSSI ( $n = 745$ ), and 10% were assessed as having SA ( $n = 225$ ). Both adolescent NSSI and SA were associated with greater risk of all outcomes as compared to patients with neither NSSI nor SA. For NSSI the adjusted HR ranged from 1.5–2.3, and for SA the adjusted HR ranged from 2.5–5.4 for alcohol/substance use disorder, subsequent episodes of self-harm and psychiatric inpatient care. The strongest associations were found for recurrent self-harm, both for patients with NSSI and SA.

## 5.4 STUDY IV -EFFICACIOUS TREATMENT COMPONENTS

In this study we used a qualitative approach to examine former DBT-A patients experiences of treatment. Out of 251 eligible former DBT-A patients, 75 participated in a semi-structured interview about their present life situation, about self-harm and was asked to elaborate on what they perceived as helpful and not helpful in treatment. They were also asked to reflect upon whether there were certain parts of DBT-A that they still used and/or found particularly meaningful. From these 75 interviews, 19 were selected for a reflexive thematic analysis aiming at assessing whether there were aspects of DBT treatment that emerged as particularly meaningful or helpful, or unhelpful or even harmful.

### 5.4.1 Results

Six key themes and two subthemes were revealed; 1) *The experience of not to be taken seriously* with the subtheme *Action speaks louder than words*, 2) *Teamwork*, 3) *Group and Structure*, 4) *Noticeable effect* with the subtheme *Skills for life—life-saving and life-changing*, 5) *Misplaced*, and 6) *Abrupt ending*. Participants shared previous experience of their suffering not being taken seriously or not being listened to. The therapist's explicit actions, demonstrating concern and belief in the patient's own capacity to change her life, was strongly appreciated and became a foundation for trust and a helpful teamwork. The skills training group was perceived as an essential part of therapy. The participants experienced that learning the DBT skills were life-saving and life-changing. Yet, some did not find DBT helpful, and for some an experience of abrupt ending of therapy became difficult.

## 6 DISCUSSION

In this thesis I have investigated the clinical presentation (study I) and subsequent outcomes (study I to III) of self-harm among help-seeking boys and girls, and important treatment aspects from some of these adolescents' point of view (study IV). The results suggest that adolescents who seek help for self-harm carry higher psychosocial burdens, have more psychiatric symptoms, and are at higher risks of adverse outcomes as compared with other help-seeking adolescents. The most vulnerable adolescents are those presenting with both self-harm and suicidality. Treatment efforts might gain from the therapist demonstrating explicit concern for the patient, targeting the youth rather than the parent, and showing trust in the adolescent's own capability to change the destructive behavior. Furthermore, skills training with peers might be of particular value for adolescents.

### 6.1.1 The clinical picture

Within a large clinical cohort ( $N = 25,161$ ) of both out- and inpatients, we compared a wide range of clinical correlates and psychosocial burdens among subgroups of patients with self-harm within a clinical population. Patients with self-harm with no suicidal ideation/attempt (SH), or with suicidal ideation/attempt (SU) only, were more burdened in terms of psychosocial problems, global functioning, and mental disorders, and had higher clinical care consumption as compared to clinical controls with no SH or SU. However, those individuals exposing both SH and SU, had the highest clinical care consumption (30.7 more visits), had more psychosocial problems and had the highest risks for mental disorders, comorbidity and psychotropic medications. A similar pattern was found in direct comparison between those with SH only and those with SH + SU. In other words, although many of the psychosocial and clinical correlates were similar in the different subgroups of self-harming patients, the associations with the negative outcomes were stronger for SH + SU. These findings are in line with previous research on populations-based cohorts (Hargus et al., 2009; Mars, Heron, Crane, Hawton, Kidger, et al., 2014) and smaller clinical cohorts (for review, see Andover et al., 2012).

The environment in which you most often meet adolescents who self-harm may affect how you perceive nonsuicidal self-injury vs suicide attempts, i.e. if they are considered as separate constructs or existing on a continuum. This is to some extent still an ongoing debate, and so far no consensus in the terminology has been found (Butler & Malone, 2013; Kapur et al., 2013; Sedgwick & Ougrin, 2019; Selby et al., 2015). At a DBT-unit or in an inpatient setting, the co-occurrence between the behaviors is high (Nock et al., 2006), and a distinction might

seem in vain at the first sight. However, if asking, for example, a DBT-patient, they will most likely make a distinction; there are self-injuring acts to feel better or at least feel something, and there are acts to end life. Yet, in an inpatient setting, this differentiation might be more difficult to make, since suicidal thoughts are more prevalent in these settings and the self-harming act might begin as an attempt to escape those suicidal thoughts but proceed to a suicide attempt. Conversely, if you meet adolescents in community-settings the co-occurrence might be less prominent, and the distinction seem more natural. Regardless of chosen terminology or construct, advanced knowledge on self-harm with and without suicidal intent in different settings, is of importance to better understand similarities and differences, and to help assess risks and adequate treatment interventions. Within a clinical setting, self-harm with and without suicidality, have several common correlates, yet, those with a combination of self-harm and suicidality are the most vulnerable.

### **6.1.2 Outcomes**

In three different longitudinal studies outcomes among help-seeking adolescents with self-harm were examined. The three studies utilized different exposures of self-harm and measured somewhat different outcomes. The chosen exposure measures affected the cohort size and length of follow up, due to more defined variables for self-harm (from SH to NSSI, SA and SI) in the clinical register over time. In study I, the exposures were self-harm (SH) with or without suicidal ideation and/or attempt (SU), or only SU (supplementary analysis), and a comparison between three different exposures (SH, SH + SU, SU) and the clinical controls (no registered SH or SU) were made. Within study II, exposure was self-harm with unknown intent, allowing for a larger cohort and lengthier follow up, and examination of sex differences in outcomes. Study III, separated suicidal ideation from suicide attempt, so the measured exposures were NSSI or SA, in a study population of patients with this type of registered ratings. Moreover, study III included NSSI and SA as time-varying covariates, taking into account that suicidal intent may vary over time.

One of the major findings from the longitudinal studies was that although within a relatively short follow up period (a median of 2.8 years, 5.8 years and 7 months, respectively), that is, already as young adults, those with a history of early self-harm were at increased risks of developing an alcohol- and/or substance use disorder (study I to III), becoming convicted due to violent or non-violent criminality (study I to II), as well as subsequent self-harm (study I to III), inpatient care (study I to III) and suicide (study II) as compared with patients at CAMHS with no self-harm.

In study I ( $N = 6,120$ ), with a median follow up period of 2.8 years, we found that although either having SH only, or SU only, had worse prognosis as compared with clinical controls in terms of alcohol use disorders (HR 2.2), recurrent care due to self-harming acts (HR 3.9), and use of anxiolytics, hypnotics, and sedatives (HR 1.4). Those adolescents displaying both SH and SU had the worst prognosis, with higher risks for all outcomes, e.g. 23 times higher risk of recurrent care due to self-harm, but also increased risks of being a recipient of social welfare (HR 2.6), having a substance use disorder (HR 4.0), and for both violent and non-violent criminality (HR 2.0; 2.1 respectively). A previous study also found self-harm (registered ICD-10 diagnosis indicating self-harm, unknown intent) to be associated with an increased risk of violent crime as compared with the general population (Sahlin et al., 2017). Our results indicate that this association might be driven by co-occurring suicidality, at least among adolescents. Furthermore, our results are consistent with previous research from population-based cohorts where SH has been found to be a risk factor of future drug use (Borschmann et al., 2017; Mars, Heron, Crane, Hawton, Lewis, et al., 2014) and subsequent self-harm, with stronger associations among those exposing self-harm with suicidal intent (Mars, Heron, Crane, Hawton, Lewis, et al., 2014), and only self-harm with suicidal intent being associated with a weaker connection with the labor market (Mars, Heron, Crane, Hawton, Lewis, et al., 2014). By utilizing clinician-ratings of self-harm with defined intent, combined with register-based outcomes, we found that also in a large clinical population, both SH and SU were associated with adverse outcomes, but the combination SH + SU had worse prognosis. However, SU included both suicidal ideation and suicidal attempts, that comprehends a wide range of behaviors comprised in one exposure variable. This makes interpretation of the results somewhat indistinct. Furthermore, SH and SU were only measured at baseline, not taking into account that the suicidal intent may vary over time. Within study III ( $N = 2,219$ ), we could differentiate suicidal ideation from suicidal behavior (SA), and we took into account that suicidal intent may vary over time, and thereby we were able to differentiate repeated NSSI only, from SA. We found that both patients with NSSI only, and SA were at increased risk of subsequent self-injury, alcohol/substance use disorder and/or psychiatric inpatient care as compared with those with no NSSI or SA, and that the risks were more pronounced among patients with SA. Considering that the majority of self-harming adolescents do not receive care from mental health services (Gillies et al., 2018), to better understand how to reach out and prevent adolescents from developing more severe NSSI with risks of SA, we need to deepen our understanding of differences in NSSI and SA. Therefore, although, there are strong links between NSSI and SA, with high co-occurrence, shared risk factors and outcomes, our findings help distinguishing between NSSI and SA, and

facilitate future research on temporal prevention, treatment interventions, as well as biological underpinnings, and guide clinicians in risk assessments and treatment planning.

Nevertheless, studies applying wider definitions of SH also have a value, not least when examining sex differences. In study II, where the exposure was SH with no definition of intent, resulting in a larger cohort (N = 110,072), and a median follow up time of 5.8 years, we found that males and females with self-harm had similar risk profiles, with increased risks for alcohol use disorder (HR 6.1 for males; 7.5 for females), substance use disorder (HR 5.0; 9.7) psychiatric inpatient care (HR 7.2; 8.5), violent criminality (HR 3.2; 5.4), non-violent criminality (HR 3.6; 5.1), and suicide (HR 4.7; 7.8), as compared with their clinical controls within the same sex. Previous research has also found that females with self-harm are at high risks for violence (Sahlin et al., 2017) and substance misuse (Fergusson et al., 2005). Possibly as an indication of an underlying borderline personality disorder, but it could also be that SH are associated with aggression and drug use independently of BPD. Irrespectively, our results indicate that SH could serve as a risk marker of problems related to impulsivity and emotion dysregulation (e.g. BPD, substance use disorder, aggressions) both in males and females.

The relatively large effect sizes for the severe outcomes found in our studies highlight the need for early and accurate treatment interventions. However, the question arises whether these interventions ought to be directed at e.g. lowering the risk of repeated NSSI, since NSSI frequency in some studies has been found to be associated with suicidal behavior (Gillies et al., 2018; Muehlenkamp et al., 2019; Victor & Klonsky, 2014), or primarily focus on preventing and treating substance use disorder, not least since substance use disorder imposes high risks of suicide (Chai et al., 2020; Michael Esang & Saeed Ahmed, 2018), or focus on improvements in self-efficacy as highlighted by BPD-patients as key outcome of treatment (DBT, (Little et al., 2018), or introduce emotion regulation skills in the school curriculum. In any case, adolescence may be a crucial moment in time for treatment interventions, not least since this is a period of time in life when parents, school or other social support can aid in help-seeking and support during treatment, but also since adolescence is a vulnerable period that can affect later outcomes (Blakemore & Mills, 2014).

### **6.1.3 Treatment**

Study IV aimed to gain a better understanding of the young patient's experience of what is helpful or not helpful in DBT-A, by searching for common denominators regarding helpful qualities, and factors that may disrupt treatment efforts. We found that acquired DBT skills affected the patient's life favorably, and that a perceived trustful relationship with the

therapist was a key component in order for the patient to feel commitment and motivation for treatment. This relationship was established by the therapist's explicit actions, e.g. showing concern for the patient, combined with treating the patient as someone who can and will do better. We also found that peer learning and teaching in skills training groups seemed particularly helpful for adolescents. The skills training group also provided an opportunity to feel social belonging. On the other hand, experiences of not having been taken seriously, or treated as too fragile, or incorrectly classified as having BPD, or having to end therapy ahead of time, were unhelpful and perhaps even harmful. Previous research has found that the relationship between the adult patient with BPD and the therapist is of great importance for treatment success (Little et al., 2018; Rudge, Feigenbaum, & Fonagy, 2017). Our findings suggest that this is also the case within a younger population with self-harm and traits of BPD. Yet, also in line with findings from a population of adult patients (Morris, Smith, & Alwin, 2014), the participants shared a history of difficulties in establishing such a relationship with health professionals. Not rarely, patients with self-harm report difficulties with identifying and expressing emotions (see Muehlenkamp, 2005), which likely paved the way for a misunderstanding of the patient's level of suffering, and perhaps this also adds to the patient's experience of not being taken seriously. In the worst-case scenario, this could lead to not seeking help the next time, or escalated self-harm. The difficulties in identifying and expressing emotions, and a possibly repeated perception of not being taken seriously, might, at least partly, explain the patient's need of the therapist's distinctly expressing understanding and caring, where words are consistent with actions, as was found in study IV. Increased knowledge among health professionals regarding the motivational factors for self-harm and the self-harming patient's difficulties in expressing and identifying emotions, could help both the patients and the professionals (Saunders et al., 2012). Yet, being cared for does not equal being treated as fragile. On the contrary, in study IV, the value of a therapist showing belief in the patient's own capacity to change their situation was highlighted. This is in line with previous research (Little et al., 2018; Perseus, Öjehagen, Ekdahl, Åsberg, & Samuelsson, 2003) showing the importance of the patient taking responsibility for therapy and making a change, as important factors in recovery. Furthermore, the sense of working in a team with the therapist seemed to have strengthened the patient's dedication for treatment, also similar to findings among studies on adult patients (Cunningham, Wolbert, & Lillie, 2004). Our analysis put forward the value of meeting others with similar problems, under regulated forms. Skills group training has previously been shown to be an important component of DBT for adults (Linehan et al., 2015; Lyng et al., 2020), and we found it to also be a highly appreciated part of treatment among adolescent patients. Meeting peers with

similar mental health history as themselves, who demonstrate progress by using skills, instill hope, counteract feelings of hopelessness, increase motivation as well as instill feelings of belonging. Notably, reduced hopelessness might be an important mediator of DBT's effect on self-harm frequency (Mehlum et al., 2019). However, DBT was not suitable for all participants. Adolescents who self-harm are a diverse group and deepened knowledge regarding predictors and moderators of treatment outcomes (such as Adrian et al., 2019) may help inform treatment planning.

Considering the high prevalence of self-harm (Gillies et al., 2018; Lim et al., 2019) and mounting evidence of the risks associated with self-harm, including the findings within this thesis, there is a substantial need of easily accessible interventions, available for adolescents in different settings (Glenn, Esposito, et al., 2019; Kothgassner et al., 2020). DBT has the strongest empirical support for treatment of self-harm in adolescents (Glenn, Esposito, et al., 2019), and as we found in our qualitative study, in line with previous qualitative studies, DBT seems to bring about treatment effects above and beyond decreasing self-harm frequency (Little et al., 2018). However, DBT is an intensive, time-consuming treatment, and the vast majority of self-harming adolescents have limited access to DBT (Kothgassner et al., 2020). Moreover, many of the self-harming adolescents may not require such extensive treatment, in particular if a preventive intervention can be achieved at an early phase of developing a self-harming behavior. Important components of DBT could be used both for development of more easily accessible interventions, as well as within general health care services and mental health services for a more efficacious care.

#### *6.1.3.1 Quantitative follow up study of former DBT-A patients*

We also aimed to do a larger uncontrolled quantitative follow up study of former DBT-A patients. Totally 251 individuals met the inclusion criteria;  $\geq 40$  visits at the DBT unit and age of  $\geq 18$  years at the time of the study. However, only 30% ( $n = 75$ ) attended the study interview. The large number of missing participants made it difficult to draw any conclusions from the data. The main part of the participants ( $n = 146$ ) could not be reached or did not show up to the scheduled interview. This can be partly understood by the age of the participants, most were in their early 20:ies, many traveling or studying in other places, but also, from traits within the target group of the treatment. This might illustrate some of the challenges in doing larger follow up studies in natural settings after DBT-A.



#### **6.1.4 Limitations**

The studies included in this thesis have limitations that need to be addressed. Register studies are based on administrative data, with predetermined variables (Thygesen & Ersbøll, 2014), constraining the data that can be collected. Our exposure measures (i.e. SH, SU, NSSI, SA), were defined using clinician ratings, and self-harming acts are often underestimated and under-reported in clinical care (Thomas et al., 2013). It is likely that many self-harming acts were unrecorded within our studies. Also, we do not know what factors influence the assessment of self-harm. Likely, some clinicians and some services may be more prone to register these ratings than others, but it could also be influenced by patient related factors other than self-harm. Furthermore, there are no estimates of reliability for the clinician assessments. In study I, we could not differentiate between suicidal ideation and suicidal attempts, and potential cross-over between the three groups across time was not explored. In study II, a sex bias in recorded self-harm could not be ruled out, also, the distinction between male and female were done by assigned sex at birth, and no conclusion regarding differences in outcomes related to gender identity could be done. Within study III, only a small proportion of patients had undergone clinician ratings, and the confidence intervals overlapped for some analyses. The follow-up time within our longitudinal studies was relatively short, varied among participants. Finally, the samples within our register studies consisted of help-seeking youths at the CAMHS, and the results may not generalize to non help-seeking populations.

Study IV also holds important limitations. There was a risk for selection bias, in that those who appreciated and found DBT valuable, could have been more willing to attend the interview. The interviewers worked at the DBT unit, which may have affected how questions were asked and answers interpreted, causing confirmation bias. Also, participants familiar with the interviewers' occupation, might have been less prone to give faulty aspects of therapy, causing information bias. In addition, no follow-up interviews were held, and the participants were not asked to provide feedback on findings.

#### **6.1.5 Future directions**

From a clinical standpoint the strong associations between self-harm and alcohol and/or substance use disorder in our young clinical population highlight the needs of regular assessments of alcohol and drug use among self-harming adolescents, and to provide appropriate treatment to prevent further continued harmful use. Not least, since alcohol and/or substance use disorder in turn also are strongly associated with both violence (Sahlin

et al., 2017) and suicide (Chai et al., 2020; Esang & Ahmed, 2018). Despite receiving more treatment in terms of medications, out- and inpatient care, the patients displaying both self-harm and suicidality, had the highest risks of alcohol/substance use disorder, but were also at risk of nonviolent and violent criminality. Although not all patients with self-harm require DBT, self-harm with co-occurring suicidality should inform assessment and treatment planning, and ought to pave the way for prompt, effective interventions, such as DBT-A. Further studies should explore the effect on the outcomes after early applied specialized treatment efforts for these patients. Furthermore, as emotion regulation difficulties can be a central underlying mechanism behind both self-harm and alcohol/substance misuse (Sloan et al., 2017), emotion regulation skills ought to be taught not only at CAMHS, but also at youth clinics, in low-threshold online interventions (such as Bjureberg et al., 2018) and be part of the school curriculum from preschool and onwards.

For youths with less severe self-harm or those who not yet have developed more severe self-harm, preventive interventions within the community settings, for example at schools or youth clinics could be helpful. Studies focusing on treatments or preventive intervention addressing youth at an early stage of self-harm are needed (C. R. Glenn, Esposito, et al., 2019). Adolescents with self-harm most frequently turn to their peers for help (Gillies et al., 2018), and adolescence is a period of social cognitive development, during which peer opinions and peer acceptance become increasingly important, and influence the adolescent behavior (Blakemore & Mills, 2014). Utilizing the influence of peers on adolescents could offer a potential treatment or prevention strategy accessible for many. We found the skills training group to be highly valued by the self-harming adolescents, and it is likely that meeting peers with similar problems and learning skills from peers, are particularly validating and helpful for adolescents. Peer led groups, within e.g. a youth clinic, supervised by experienced DBT-therapists or equivalent, could offer a treatment intervention, easily accessible for many and offered at an early stage of self-harming, hopefully preventing further negative progress. However, with knowledge about the risks of exposure to self-harm (Mars et al., 2019a, 2019b), as well as risk for substance use among self-harming adolescents (Moran et al., 2012), this need to be carefully monitored and further studies are needed.

Moreover, self-harm by an adolescent or child causes major emotional distress to the parents or other key adults and family members, and the needs of support and guidance to the parents have been pointed out (Byrne et al., 2008; Ferrey et al., 2016; Fu et al., 2020; Krysinaka et al., 2020). Parent training/education as a treatment element has been found to be associated with positive outcomes in adolescents with self-harming behaviors (Brent, 2019; Brent et al.,

2013; Glenn, Esposito, et al., 2019; Ougrin et al., 2015). Psychoeducational interventions directed at parents or other family members, as well as specific parent training, already in an early phase of self-harm, support the families and may have the potential to decrease the risk of further adverse outcomes for the adolescent (Brent, 2019). Future studies should explore how parents and other key adults experience parent skills training groups in DBT as well as previous care contacts, to inform further development of an early stage support to the families.

Research should aim at developing efficacious aid for family, friends and school personnel to help the adolescent who self-harm. Furthermore, the research community need to develop and evaluate specialized interventions that can be promptly available when these measures are not enough.

## **7 CONCLUSION**

Boys and girls who contact the CAMHS with self-harm, with or without suicidal intent, are burdened patient groups that need appropriate care and assessment, including prevention and treatment of alcohol and substance misuse. Suicidality need to be regularly assessed, and signals highly increased risks for future self-injury, alcohol/substance use disorder, criminality and suicidal death. Interventions that lower the risk of future adverse outcomes are necessary. Young patients with self-harm, can be strongly motivated, and work hard, to improve their well-being and pursue a life worth living. DBT-A comprise components and approaches that are valued by the young patient. Teaching and learning from peers might be of particular value and importance among adolescents.



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